1: Am J Clin Nutr 2002 Dec;76(6):1191-201 Related Articles, Links

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Beneficial role of dietary phytoestrogens in obesity and diabetes.

Bhathena SJ, Velasquez MT.

Phytonutrients Laboratory, Beltsville Human Nutrition Research Center, Agricultural Research Service, US Department of Agriculture, Beltsville, MD 20705, USA. bhathens@ba.ars.usda.gov

Evidence is emerging that dietary phytoestrogens play a beneficial role in obesity and diabetes. Nutritional intervention studies performed in animals and humans suggest that the ingestion of soy protein associated with isoflavones and flaxseed rich in lignans improves glucose control and insulin resistance. In animal models of obesity and diabetes, soy protein has been shown to reduce serum insulin and insulin resistance. In studies of human subjects with or without diabetes, soy protein also appears to moderate hyperglycemia and reduce body weight, hyperlipidemia, and hyperinsulinemia, supporting its beneficial effects on obesity and diabetes. However, most of these clinical trials were relatively short and involved a small number of patients. Furthermore, it is not clear whether the beneficial effects of soy protein and flaxseed are due to isoflavones (daidzein and genistein), lignans (matairesinol and secoisolariciresinol), or some other component. Isoflavones and lignans appear to act through various mechanisms that modulate pancreatic insulin secretion or through antioxidative actions. They may also act via estrogen receptor-mediated mechanisms. Some of these actions have been shown in vitro, but the relevance of these studies to in vivo disease is not known. The diversity of cellular actions of isoflavones and lignans supports their possible beneficial effects on various chronic diseases. Further investigations are needed to evaluate the long-term effects of phytoestrogens on obesity and diabetes mellitus and their associated possible complications.

Publication Types:
- Review
- Review, Tutorial

PMID: 12450882 [PubMed - indexed for MEDLINE]

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Synthesis of (-)-matairesinol, (-)-enterolactone, and (-)-enterodiol from the natural lignan hydroxymatairesinol.
Org Lett. 2003 Feb 20;5(4):491-3.
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Antioxidant and antitumor effects of hydroxymatairesinol (HM-3000, HMR), a lignan isolated from the knots of spruce.
Eur J Cancer Prev. 2002 Aug;11 Suppl 2:S48-57.
PMID: 12570335 [PubMed - indexed for MEDLINE]

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Structural determinants of plant lignans for the formation of enterolactone in vivo.
J Chromatogr B Analyt Technol Biomed Life Sci. 2002 Sep 25;777(1-2):311-9.
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Nutr Cancer. 2001;41(1-2):82-90.
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7: Heinonen S, Nurmi T, Liukkonen K, Poutanen K, Wahala K, Deyama T, Nishibe S, Adlercreutz H. Related Articles, Links

In vitro metabolism of plant lignans: new precursors of mammalian lignans enterolactone and enterodiol.
J Agric Food Chem. 2001 Jul;49(7):3178-86.
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8: Xia ZQ, Costa MA, Proctor J, Davin LB, Lewis NG. Related Articles, Links

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Phytochemistry. 2000 Nov;55(6):537-49.
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Chemopreventive activity of crude hydroxsymatairesinol (HMR) extract in Apc(Min) mice.
Cancer Lett. 2000 Dec 20;161(2):253-8.
PMID: 11090976 [PubMed - indexed for MEDLINE]

10: Oikannen SI, Pajari AM, Mutanen M. Related Articles, Links

Chemopreventative activity of crude hydroxymatairesinol (HMR) extract in Apc(Min) mice [corrected].
Cancer Lett. 2000 Oct 31;159(2):183-7.
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Hydroxymatairesinol, a novel enterolactone precursor with antitumor properties from coniferous tree (Picea abies).
Nutr Cancer. 2000;36(2):207-16.
PMID: 10890032 [PubMed - indexed for MEDLINE]

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1: J Agric Food Chem 2000 Jul;48(7):2910-9 Related Articles, Links

Oxidative metabolites of the mammalian lignans enterodiol and enterolactone in rat bile and urine.

Niemeyer HB, Honig D, Lange-Bohmer A, Jacobs E, Kulling SE, Metzler M.

Institute of Food Chemistry, Department of Chemistry, University of Karlsruhe, P.O. Box 6980, GY-76128 Karlsruhe, Germany.

Recent studies have shown that the mammalian lignans enterodiol (END) and enterolactone (ENL) are biotransformed in vitro by hepatic microsomes from rats and humans to various metabolites carrying one additional hydroxy group either at the aromatic or at the aliphatic moiety. To clarify whether these metabolites are also formed in vivo, each lignan was administered intraduodenally at a dose of 10 mg/kg of bw to bile duct-catheterized female Wistar rats and the 6 h bile analyzed by HPLC and GC-MS. With END-dosed rats, three products of aromatic and two of aliphatic monohydroxylation were found, whereas six aromatic and five aliphatic monohydroxylated biliary metabolites were detected after administration of ENL. The metabolites hydroxylated at the aromatic rings were unequivocally identified by comparison with synthetic reference compounds. The structures of the in vivo metabolites arising from aliphatic hydroxylation could not be completely elucidated; they were identical with some of the formerly reported microsomal products according to GC retention times and mass spectra. Significant amounts of most of the metabolites of the mammalian lignans identified in bile were also found in the urine of female rats after oral administration of 10 mg/kg of bw END or ENL and in the urine of female and male Wistar rats after they had been fed a diet containing 5% flaxseed. Thus, the mammalian lignans END and ENL give rise to several hydroxylated metabolites in vivo, which may contribute to the biological effects of these important food constituents.

PMID: 10898644 [PubMed - indexed for MEDLINE]

1: Mol Cell Biochem 1999 Dec;202(1-2):91-100 Related Articles, Links

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Antioxidant activity of the flaxseed lignan secoisolariciresinol diglycoside and its mammalian lignan metabolites enterodiol and enterolactone.

Kitts DD, Yuan YV, Wijewickreme AN, Thompson LU.

Food, Nutrition, and Health, Faculty of Agricultural Science, University of British Columbia, Vancouver, Canada.

The antioxidant activities of the flaxseed lignan secoisolariciresinol diglycoside (SDG) and its mammalian lignan metabolites, enterodiol (ED) and enterolactone (EL), were evaluated in both lipid and aqueous in vitro model systems. All three lignans significantly ($p < or = 0.05$) inhibited the linoleic acid peroxidation at both 10 and 100 microM over a 24-48 h of incubation at 40 degrees C. In a deoxyribose assay, which evaluates the non site-specific and site-specific Fenton reactant-induced *OH scavenging activity, SDG demonstrated the weakest activity compared to ED and EL at both 10 and 100 microM; the greatest *OH scavenging for ED and EL was observed at 100 microM in both assays. The incubation of pBR322 plasmid DNA with Fenton reagents together with SDG, ED or EL showed that the inhibition of DNA scissions was concentration dependent. The greatest non site-specific activity of lignans was at 100 microM, thus, confirming the results of the deoxyribose test. In contrast, the protective effect of SDG and EL in the site-specific assay was lost and that of ED was minimal. Therefore, the results indicate a structure-activity difference among the three lignans with respect to specific antioxidant efficacy. All three lignans did not exhibit reducing activity compared to ascorbic acid, therefore, did not possess indirect prooxidant activity related to potential changes in redox state of transition metals. The efficacy of SDG and particularly the mammalian lignans ED and EL to act as antioxidants in lipid and aqueous in vitro model systems, at relatively low concentrations (i.e. 100 microM), potentially achievable in vivo, is an evidence of a potential anticarcinogenic mechanism of flaxseed lignan SDG and its mammalian metabolites ED and EL.

PMID: 10705999 [PubMed - indexed for MEDLINE]

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1: J Pharm Pharmacol 1992 Oct;44(10):859-61 Related Articles, Links

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Effect of mammalian lignans on fMLP-induced oxidative bursts in human polymorphonuclear leucocytes.

Morikawa M, Fukuchi K, Inoue M, Tsuboi M.

Department of Pharmacology, Tokyo College of Pharmacy, Japan.

We examined the effects of mammalian lignans, enterolactone, prestegane B and 2,3-dibenzylbutane-1,4-diol (DBB) on superoxide production and luminol-dependent chemiluminescence (LCL) response in human polymorphonuclear leucocytes (PMNs). The three lignans had no direct effect on the responses of human PMNs. DBB and prestegane B enhanced the superoxide production and LCL response induced by formylmethionyl-leucyl-phenylalanine (fMLP), but enterolactone inhibited fMLP-induced effects. The effects of DBB were stronger than those of prestegane B and the effects of DBB were inhibited by bromophenacyl bromide, mepacrine, N-(6-aminophenyl)-5-chloro-1-naphthalene, sulphonamide and trifluoroperazine, but not by gossypol, nordihydroguaretic acid, indomethacin, staurosporine, 1-(5-isoquinolinesulphonyl)-2-methylpiperazine dihydrochloride or (R,S)-2-methoxy-3-(octadecyl-carbamoyloxy)-propyl-2-(2-thiazoli o)-ethylphosphate. These results suggest that DBB primes the responses of human PMNs, and the priming effect is caused by the activation of phospholipase A2--and Ca(2+)-calmodulin-pathways, but not by the activation of lipoxygenase, cyclo-oxygenase and protein kinase C or by the release of platelet activating factor.

PMID: 1360514 [PubMed - indexed for MEDLINE]

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1: Am J Clin Nutr 1994 Jul;60(1):122-8 Related Articles, Links

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Urinary lignan and isoflavonoid excretion in premenopausal women consuming flaxseed powder.

Lampe JW, Martini MC, Kurzer MS, Adlercreutz H, Slavin JL.

Department of Food Science and Nutrition, University of Minnesota, St Paul 55108.

Lignans and isoflavonoid phytoestrogens, produced from plant precursors by colonic bacteria, may protect against certain cancers. We examined the effects of flaxseed consumption on urinary lignans and isoflavonoids. Eighteen women consumed their usual omnivorous diets for three menstrual cycles and their usual diets supplemented with flaxseed powder (10 g/d) for three cycles in a randomized crossover design. Three-day urine samples from follicular and luteal phases were analyzed for lignans and isoflavonoids by isotope-dilution gas chromatography--mass spectrometry. Excretion of the lignans enterodiol and enterolactone increased with flaxseed from 1.09 +/- 1.08 and 3.16 +/- 1.47 to 19.48 +/- 1.10 and 27.79 +/- 1.50 mumol/d, respectively ($P < 0.0002$). Enterodiol and enterolactone excretion varied among subjects in response to flaxseed (3- to 285-fold increase). There were no differences in excretion of isoflavonoids (daidzein, genistein, equol, and O-desmethylangolensin) or the lignan matairesinol with flaxseed. Excretion was not altered by phase of menstrual cycle or duration of flaxseed consumption.

Publication Types:
- Clinical Trial
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PMID: 8017326 [PubMed - indexed for MEDLINE]

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1: Drugs Exp Clin Res 2002;28(4):133-45 Related Articles, Links

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Inhibitory effects of zafirlukast on respiratory bursts of human neutrophils.

Braga PC, Dal Sasso M, Dal Negro R.

Center of Respiratory Pharmacology, Department of Pharmacology, School of Medicine, University of Milan, Milan, Italy. bragapc@mailserver.unimi.it

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The effects of zafirlukast, a cysteinyl-leukotriene receptor antagonist, on the generation of the reactive oxygen species (ROS) released during respiratory bursts of human polymorphonuclear neutrophils (PMNs) is still unknown. The aim of this study was to investigate the ability of zafirlukast to interfere with the respiratory burst of PMNs. Respiratory burst responses of PMNs were investigated by luminol-amplified chemiluminescence (LACL) using particulate (Candida albicans and zymosan) and soluble stimulants [N-formyl-methionylleucyl-phenylalanine (fMLP) and phorbol 12 myristate 13 acetate (PMA)]. When incubated with PMNs for 10 min at concentrations ranging from 5 x 10(-9) M to 5 x 10(-6) M, zafirlukast did not significantly affect the respiratory bursts of PMNs induced by either the particulate or soluble stimuli. However, after incubation for 60 min, it did reduce the respiratory bursts of PMNs in a concentration-related fashion when the PMNs were stimulated with fMLP, and at a concentration of 5 x 10(-6) M when the stimulus was PMA. No significant effects were seen when the PMNs were challenged with particulate stimuli. Zafirlukast is able to interfere with the activation of the PMNs respiratory burst induced by soluble stimulants. The different behavior determined by different times of contact and different stimuli opens the way to interpretations concerning the antioxidant effect of zafirlukast.

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PMID: 12512231 [PubMed - in process]

1: Gerontology 1998;44(4):192-7 Related Articles, Links

Influence of age on oxidative bursts (chemiluminescence) of polymorphonuclear neutrophil leukocytes.

Braga PC, Sala MT, Dal Sasso M, Mancini L, Sandrini MC, Annoni G.

Department of Pharmacology, University of Milan, School of Medicine, Italy.

The release of reactive oxygen species (ROS) during neutrophil oxidative bursts is the last of a sequence of different steps leading to the neutralization of pathogen microorganisms. Using luminol-amplified chemiluminescence (LACL), the oxidative burst activity of neutrophils in elderly people (> or = 75 years) was compared with that in younger controls (39 years on average) after activation with both particulate (Candida albicans) and soluble (formyl-methionyl-leucyl-phenylalanine; fMLP) stimulants. After Candida stimulation, a reduction in LACL was observed in the elderly subjects in comparison with the controls, but the difference did not reach statistical significance. After fMLP stimulation, the reduction in LACL was significant, thus suggesting that the Candida pathway of chemiluminescence production seems to be less affected than the fMLP pathway. This finding raises questions concerning the complex differences in the pathways of cell killing and ROS generation, and their efficacy in the elderly. Various possible explanations are discussed, all of which need further investigation.

PMID: 9657078 [PubMed - indexed for MEDLINE]

1: Eur J Cancer Prev 2002 Aug;11 Suppl 2:S48-57 Related Articles, Links

Antioxidant and antitumor effects of hydroxymatairesinol (HM-3000, HMR), a lignan isolated from the knots of spruce.

Kangas L, Saarinen N, Mutanen M, Ahotupa M, Hirsinummi R, Unkila M, Perala M, Soininen P, Laatikainen R, Korte H, Santti R.

Hormos Nutraceutical Ltd, Turku, Finland.

The antioxidant properties of hydroxymatairesinol (HM-3000) were studied in vitro in lipid peroxidation, superoxide and peroxyl radical scavenging, and LDL-oxidation models in comparison with the known synthetic antioxidants Trolox (a water-soluble vitamin E derivative), butylated hydroxyanisol (BHA) and butylated hydroxytoluene (BHT). On a molar basis HM-3000 was a more effective antioxidant than Trolox in all assays and more effective than BHT or BHA in lipid peroxidation and superoxide scavenging test. The in vivo antioxidative effect (evaluated as the weight gain of C57BL/6J mice fed an alpha-tocopherol-deficient diet) of HM-3000 (500 mg/kg per day) was comparable to that of DL-alpha-tocopherol (766 mg/kg per day). The antitumor activity of HM-3000 was studied in dimethylbenz[a]anthracene (DMBA)-induced rat mammary cancer. HM-3000 had a statistically significant inhibitory effect on tumor growth. Prevention of tumor formation was also evaluated in the Apc(Min) mice model, which develops intestinal polyps spontaneously. HM-3000 was given in diet at 30 mg/kg per day and decreased the formation of polyps and prevented beta-catenin accumulation into the nucleus, the pathophysiological hallmark of polyp formation in this mouse model. In short-term toxicity studies (up to 28 days) HM-3000 was essentially non-toxic when given p.o. to rats and dogs (daily doses up to 2000 and 665 mg/kg, respectively); HM-3000 was shown to be well absorbed (> 50% of the dose) and rapidly eliminated. In human studies HM-3000 has been given in single doses up to 1350 mg to healthy male volunteers without treatment-related adverse events. Rapid absorption from the gastrointestinal tract and partial metabolism to enterolactone in humans was demonstrated. In summary, HM-3000 is a safe, novel enterolactone precursor lignan with antioxidant and antitumor properties.

PMID: 12570335 [PubMed - indexed for MEDLINE]

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RN   380448-77-1  REGISTRY
CN   2(3H)-Furanone, dihydro-4-[(R)-hydroxy(4-hydroxy-3-
     methoxyphenyl)methyl]-3-[(4-hydroxy-3-methoxyphenyl)methyl]-, (3S,4S)-rel-
     (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   (.+-.)-7'-Allohydroxymatairesinol
FS   STEREOSEARCH
MF   C20 H22 O7
SR   CA
LC   STN Files:   CA, CAPLUS

Relative stereochemistry.
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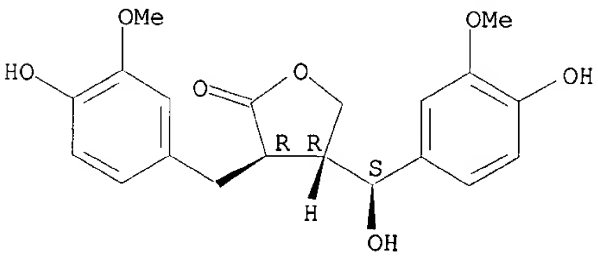


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REFERENCE   1:  136:37434

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RN   380448-76-0  REGISTRY
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     (9CI)  (CA INDEX NAME)
OTHER NAMES:
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SR CA
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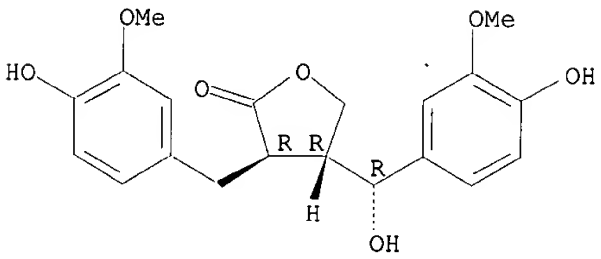
Relative stereochemistry.



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REFERENCE 1: 136:37434

L130 ANSWER 3 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN 347359-71-1 REGISTRY
CN **2(3H)-Furanone, dihydro-4-[hydroxy(4-hydroxy-3-methoxyphenyl)methyl]-3-[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)- (9CI)** (CA INDEX NAME)
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MF **C20 H22 O7**
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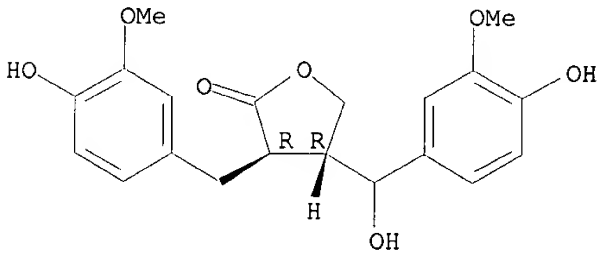
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER

Absolute stereochemistry.



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REFERENCE 3: 137:337724

REFERENCE 4: 135:89908

L130 ANSWER 4 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN 185254-87-9 REGISTRY

CN **2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3S,4S)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3S-trans)-**
OTHER NAMES:
CN (+)-Enterolactone
FS STEREOSEARCH
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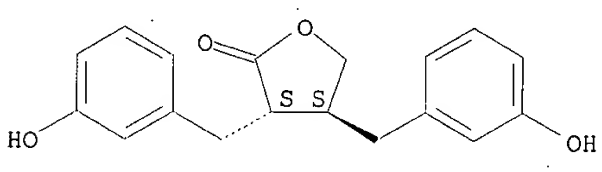
Absolute stereochemistry. Rotation (+).



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REFERENCE 2: 132:279044

REFERENCE 3: 126:74627

L130 ANSWER 5 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN 148409-36-3 REGISTRY
CN **2(3H)-Furanone, dihydro-3,4-bis[(4-hydroxy-3-methoxyphenyl)methyl]-, (3S,4S)- (9CI)** (CA INDEX NAME)
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CN **2(3H)-Furanone, dihydro-3,4-bis[(4-hydroxy-3-methoxyphenyl)methyl]-, (3S-trans)-**
OTHER NAMES:
CN (+)-Matairesinol
FS STEREOSEARCH
MF **C20 H22 O6**
SR CA
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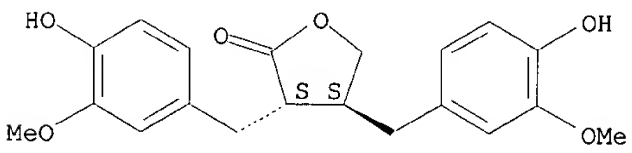
Absolute stereochemistry.



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REFERENCE 2: 136:337784

REFERENCE 3: 136:131515

REFERENCE 4: 133:347084

REFERENCE 5: 128:255172

REFERENCE 6: 127:202873

REFERENCE 7: 124:235157

REFERENCE 8: 121:31155

REFERENCE 9: 119:24655

L130 ANSWER 6 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN 120409-94-1 REGISTRY
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OTHER CA INDEX NAMES:
CN **2(3H)-Furanone, dihydro-3,4-bis[(4-hydroxy-3-methoxyphenyl)methyl]-, trans-**
FS STEREOSEARCH
DR 42298-55-5, 346419-32-7
MF **C20 H22 O6**
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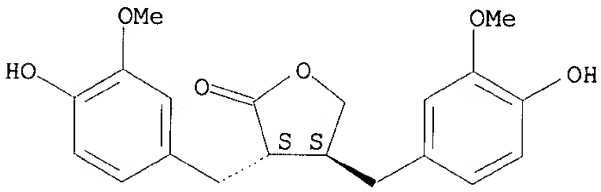
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT
(*File contains numerically searchable property data)

Relative stereochemistry.



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REFERENCE 2: 135:92476

REFERENCE 3: 134:366723

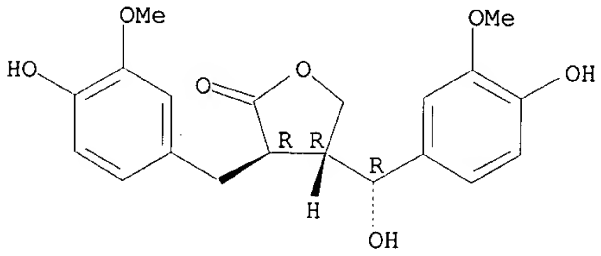
REFERENCE 4: 116:41173

REFERENCE 5: 110:212466

L130 ANSWER 7 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN 81623-30-5 REGISTRY
CN **2(3H)-Furanone, dihydro-4-[(R)-hydroxy(4-hydroxy-3-methoxyphenyl)methyl]-3-[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)-**

(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **2(3H)-Furanone, dihydro-4-[hydroxy(4-hydroxy-3-methoxyphenyl)methyl]-3-[(4-hydroxy-3-methoxyphenyl)methyl]-, [3R-[3.alpha.,4.beta.(R*)]]-**
OTHER NAMES:
CN (-)-allo-Hydroxymatairesinol
CN 5-Allohydroxymatairesinol
CN Allohydroxymatairesinol
FS STEREOSEARCH
MF **C20 H22 O7**
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

14 REFERENCES IN FILE CA (1957 TO DATE)
14 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:4458

REFERENCE 2: 135:166155

REFERENCE 3: 133:235125

REFERENCE 4: 132:312816

REFERENCE 5: 132:310001

REFERENCE 6: 132:33212

REFERENCE 7: 131:58090

REFERENCE 8: 129:246685

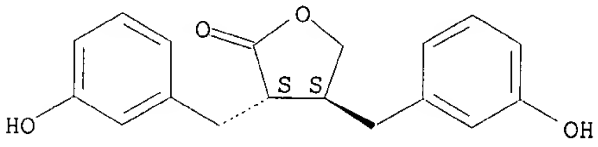
REFERENCE 9: 124:292625

REFERENCE 10: 123:138812

L130 ANSWER 8 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **78473-71-9** REGISTRY
CN **2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-rel- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, trans-**
OTHER NAMES:
CN (.+-.)-enterolactone
CN **Enterolactone**
CN HPMF
CN trans-2,3-Bis(3-hydroxybenzyl)-.gamma.-butyrolactone

FS STEREOSEARCH
DR **76721-88-5, 82580-69-6, 110872-76-9**
MF **C18 H18 O4**
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CSCHEM, DDFU, DRUGU, EMBASE, MRCK*, NAPRALERT, PROMT, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

168 REFERENCES IN FILE CA (1957 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
167 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:163617

REFERENCE 2: 138:136423

REFERENCE 3: 138:103060

REFERENCE 4: 138:72572

REFERENCE 5: 138:66763

REFERENCE 6: 138:51252

REFERENCE 7: 138:13762

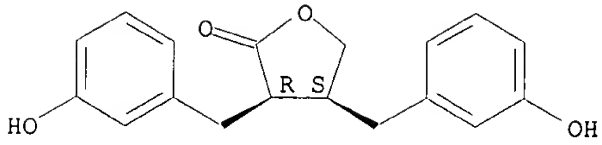
REFERENCE 8: 137:384977

REFERENCE 9: 137:337200

REFERENCE 10: 137:324765

L130 ANSWER 9 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **77756-21-9** REGISTRY
CN **2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, cis- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, cis-(.+-.)-**
FS STEREOSEARCH
MF **C18 H18 O4**
LC STN Files: BEILSTEIN*, CA, CAPLUS, USPATFULL
(*File contains numerically searchable property data)

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1957 TO DATE)
3 REFERENCES IN FILE CAPLUS (1957 TO DATE)

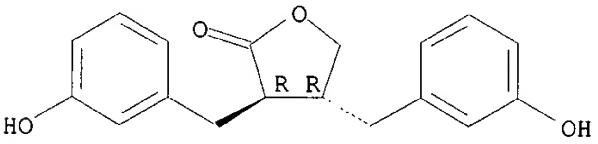
REFERENCE 1: 96:162321

REFERENCE 2: 96:85409

REFERENCE 3: 95:24670

L130 ANSWER 10 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **77756-20-8** REGISTRY
CN **2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-(9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R-trans)-**
OTHER NAMES:
CN (-)-Enterolactone
CN (-)-Interolactone
FS STEREOSEARCH
MF **C18 H18 O4**
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

13 REFERENCES IN FILE CA (1957 TO DATE)
13 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:237931

REFERENCE 2: 136:247437

REFERENCE 3: 134:97634

REFERENCE 4: 132:279044

REFERENCE 5: 131:73494

REFERENCE 6: 126:74627

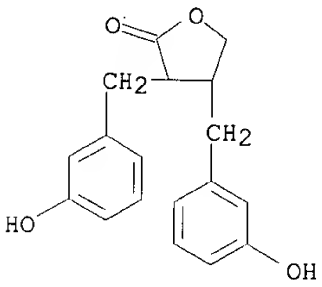
REFERENCE 7: 124:8482

REFERENCE 8: 121:280455

REFERENCE 9: 117:69644

REFERENCE 10: 110:75111

L130 ANSWER 11 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN 76543-15-2 REGISTRY
CN **2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]- (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN Compound 180/442
FS 3D CONCORD
MF **C18 H18 O4**
CI COM
LC STN Files: BEILSTEIN*, CA, CANCERLIT, CAPLUS, MEDLINE, TOXCENTER
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 110:1066

REFERENCE 2: 95:39713

REFERENCE 3: 95:39646

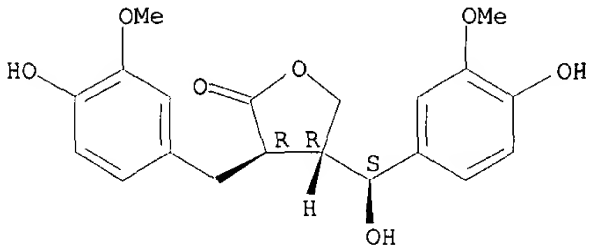
REFERENCE 4: 94:189096

REFERENCE 5: 94:80880

L130 ANSWER 12 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN 20268-71-7 REGISTRY
CN **2(3H)-Furanone, dihydro-4-[(S)-hydroxy(4-hydroxy-3-methoxyphenyl)methyl]-3-[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)-(9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2(3H)-Furanone, dihydro-4-(.alpha.-hydroxyvanillyl)-3-vanillyl- (8CI)
CN **2(3H)-Furanone, dihydro-4-[hydroxy(4-hydroxy-3-methoxyphenyl)methyl]-3-[(4-hydroxy-3-methoxyphenyl)methyl]-, [3R-[3.alpha.,4.beta.(S*)]]-**
OTHER NAMES:
CN .alpha.-Hydroxymatairesinol
CN 5-Hydroxymatairesinol
CN **Hydroxymatairesinol**

FS STEREOSEARCH
DR 29764-17-8
MF **C20 H22 O7**
LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, IPA, NAPRALERT, PIRA, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

44 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
44 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:12731

REFERENCE 2: 138:4458

REFERENCE 3: 137:216291

REFERENCE 4: 136:387621

REFERENCE 5: 136:380145

REFERENCE 6: 135:132430

REFERENCE 7: 134:202501

REFERENCE 8: 134:25175

REFERENCE 9: 133:344260

REFERENCE 10: 133:286508

L130 ANSWER 13 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **9003-99-0** REGISTRY
CN Peroxidase (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Baylase RP
CN Biobake soy
CN Biobake Wheat
CN Coniferyl alcohol peroxidase
CN E.C. 1.11.1.7
CN Enzylon OL 50
CN Eosinophil peroxidase
CN Extensin peroxidase
CN Guaiacol peroxidase
CN Guaiacolase
CN Heme peroxidase
CN Lactoperoxidase

CN Manganese-dependent peroxidase
CN Mn-dependent peroxidase
CN MPO
CN Myeloperoxidase
CN Novozym 502
CN Oxyperoxidase
CN PEO-131
CN Peroxidase 51004
CN Protoheme peroxidase
CN Pyrocatechol peroxidase
CN Pyrogallol peroxidase
CN Scavengase p20
CN Scopoletin peroxidase
CN SP 502
CN Thiocyanate peroxidase
CN Thiol peroxidase
CN Verdoperoxidase
DR 9013-92-7, 9039-19-4, 191289-36-8
MF Unspecified
CI COM, MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, TOXCENTER, ULIDAT, USPAT2, USPATFULL
Other Sources: EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
31109 REFERENCES IN FILE CA (1957 TO DATE)
2125 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
31158 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:292375

REFERENCE 2: 138:286608

REFERENCE 3: 138:286499

REFERENCE 4: 138:286407

REFERENCE 5: 138:286377

REFERENCE 6: 138:285706

REFERENCE 7: 138:285537

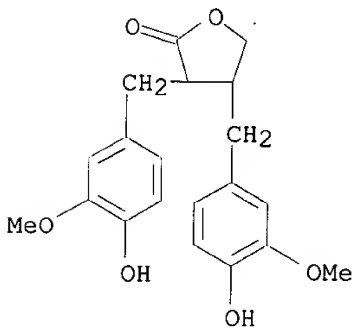
REFERENCE 8: 138:285498

REFERENCE 9: 138:285022

REFERENCE 10: 138:285021

L130 ANSWER 14 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN 7471-01-4 REGISTRY
CN **2(3H)-Furanone, dihydro-3,4-bis[(4-hydroxy-3-methoxyphenyl)methyl]-(9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2(3H)-Furanone, dihydro-3,4-divanillyl- (8CI)
CN Butyric acid, 4-hydroxy-2,3-divanillyl-, .gamma.-lactone (7CI)
FS 3D CONCORD
MF **C20 H22 O6**
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXCENTER

(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1957 TO DATE)
5 REFERENCES IN FILE CAPLUS (1957 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 136:244409

REFERENCE 2: 135:55452

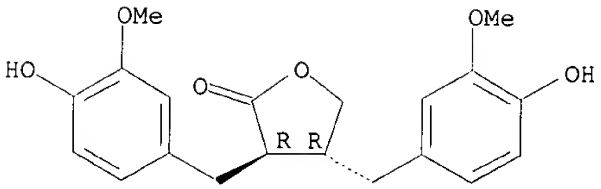
REFERENCE 3: 126:343483

REFERENCE 4: 70:75057

REFERENCE 5: 66:77100

L130 ANSWER 15 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **580-72-3** REGISTRY
CN **2(3H)-Furanone, dihydro-3,4-bis[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **2(3H)-Furanone, dihydro-3,4-bis[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R-trans)-**
CN 2(3H)-Furanone, dihydro-3,4-divanillyl- (8CI)
CN **Matairesinol (6CI)**
OTHER NAMES:
CN (-)-Matairesinol
CN (8R,8'R)-(-)-Matairesinol
FS STEREOSEARCH
DR 41328-88-5
MF **C20 H22 O6**
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CSCHEM, DDFU, DRUGU, EMBASE, MEDLINE, NAPRALERT, PIRA, PROMT, SPECINFO, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

214 REFERENCES IN FILE CA (1957 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
215 REFERENCES IN FILE CAPLUS (1957 TO DATE)
6 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:268405

REFERENCE 2: 138:237931

REFERENCE 3: 138:163104

REFERENCE 4: 138:108457

REFERENCE 5: 138:103218

REFERENCE 6: 138:72572

REFERENCE 7: 138:51252

REFERENCE 8: 138:19704

REFERENCE 9: 137:352162

REFERENCE 10: 137:351939

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 16:21:15 ON 06 MAY 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 6 May 2003 VOL 138 ISS 19
FILE LAST UPDATED: 5 May 2003 (20030505/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot l128

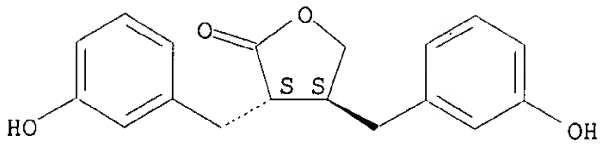
L128 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN 2003:166959 HCAPLUS
DN 138:163617
TI Forsythia extracts containing pinoresinol as drugs and health foods for treatment of cancer and menopause disorders
IN Seibu, Kazumi; Herman, Adlercreutz; Shiba, Shunichi; Yori, Haruki
PA Tama Biochemical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61K035-78
ICS A23F003-14; A23L001-30; A61K031-34; A61P015-12; A61P019-10; A61P035-00; C07D493-04
CC 1-12 (Pharmacology)
Section cross-reference(s): 17
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2003063971	A2	20030305	JP 2001-253043	20010823
PRAI JP 2001-253043		20010823		

AB Forsythia exts. contg. pinoresinol are claimed as drugs and health foods for treatment of cancer and menopause disorders, including osteoporosis. Enterodiol and **enterolactone** are identified as fecal metabolites of pinoresinol.
ST Forsythia ext pinoresinol health food cancer menopause disorder
IT Antitumor agents
Forsythia
Forsythia suspensa
Health food
Human
Neoplasm
Osteoporosis
Uterus, neoplasm
(Forsythia exts. contg. pinoresinol as drugs and health foods for treatment of cancer and menopause disorders)
IT **Menopause**
(disorder; Forsythia exts. contg. pinoresinol as drugs and health foods for treatment of cancer and menopause disorders)
IT Mammary gland
Prostate gland
(neoplasm; Forsythia exts. contg. pinoresinol as drugs and health foods for treatment of cancer and menopause disorders)
IT **78473-71-9, Enterolactone** 80226-00-2, Enterodiol
RL: ANT (Analyte); **PKT (Pharmacokinetics)**; ANST (Analytical study); BIOL (Biological study)
(Forsythia exts. contg. pinoresinol as drugs and health foods for treatment of cancer and menopause disorders)
IT 487-36-5P,, Pinoresinol
RL: PKT (Pharmacokinetics); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Forsythia exts. contg. pinoresinol as drugs and health foods for treatment of cancer and menopause disorders)
IT **78473-71-9, Enterolactone**
RL: ANT (Analyte); **PKT (Pharmacokinetics)**; ANST (Analytical study); BIOL (Biological study)
(Forsythia exts. contg. pinoresinol as drugs and health foods for treatment of cancer and menopause disorders)
RN 78473-71-9 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-rel-

(9CI) (CA INDEX NAME)

Relative stereochemistry.



L128 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:923545** HCAPLUS
DN **138:136452**
TI Beneficial role of dietary phytoestrogens in obesity and diabetes
AU Bhathena, Sam J.; Velasquez, Manuel T.
CS Phytonutrients Laboratory. Beltsville Human Nutrition Research Center, Agricultural Research Service, US Department of Agriculture, Beltsville, MD, 20705, USA
SO American Journal of Clinical Nutrition (2002), 76(6), 1191-1201
CODEN: AJCNAC; ISSN: 0002-9165
PB American Society for Clinical Nutrition
DT Journal
LA English
CC 18-7 (Animal Nutrition)
AB Evidence is emerging that dietary phytoestrogens play a beneficial role in obesity and diabetes. Nutritional intervention studies performed in animals and humans suggest that the ingestion of soy protein assocd. with isoflavones and flaxseed rich in lignans improves glucose control and insulin resistance. In animal models of obesity and diabetes, soy protein has been shown to reduce serum insulin and insulin resistance. In studies of human subjects with or without diabetes, soy protein also appears to moderate hyperglycemia and reduce body wt., hyperlipidemia, and hyperinsulinemia, supporting its beneficial effects on obesity and diabetes. However, most of these clin. trials were relatively short and involved a small no. of patients. Furthermore, it is not clear whether the beneficial effects of soy protein and flaxseed are due to isoflavones (daizein and genistein), lignans (**matairesinol** and secoisolariciresinol), or some other component. Isoflavones and lignans appear to act through various mechanisms that modulate pancreatic insulin secretion or through antioxidative actions. They may also act via estrogen receptor-mediated mechanisms. Some of these actions have been shown in vitro, but the relevance of these studies to in vivo disease is not known. The diversity of cellular actions of isoflavones and lignans supports their possible beneficial effects on various chronic diseases. Further investigations are needed to evaluate the long-term effects of phytoestrogens on obesity and diabetes mellitus and their assocd. possible complications.
ST phytoestrogen diet obesity diabetes
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dietary; phytoestrogens in relation to obesity and diabetes)
IT Flavones
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(isoflavones; phytoestrogens in relation to obesity and diabetes)
IT **Diabetes mellitus**
Flaxseed
Obesity
Soybean (Glycine max)
(phytoestrogens in relation to obesity and diabetes)
IT Lignans
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(phytoestrogens in relation to obesity and diabetes)
IT Estrogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phytoestrogens; phytoestrogens in relation to obesity and diabetes)
IT 50-99-7, Glucose, biological studies 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phytoestrogens in relation to obesity and diabetes)
RE.CNT 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Abler, A; J Biol Chem 1992, V267, P3946 HCAPLUS
(2) Adlercreutz, H; Am J Clin Nutr 1991, V54, P1093 HCAPLUS
(3) Adlercreutz, H; Ann Med 1997, V2, P95
(4) Adlercreutz, H; J Steroid Biochem 1986, V25, P791 HCAPLUS
(5) Adlercreutz, H; Lancet 1993, V342, P1209 MEDLINE
(6) Adlercreutz, H; Scand J Clin Lab Invest 1993, V53(supl), P5
(7) Ahmed, M; Diabetologia 1976, V12, P61 HCAPLUS
(8) Akiyama, T; J Biol Chem 1987, V262, P5592 HCAPLUS
(9) Anderson, J; Am J Clin Nutr 1998, V68(suppl), P1347S
(10) Anderson, J; Balliere's Clin Endocrinol Metab 1998, V12, P543 MEDLINE
(11) Anthony, M; Am J Clin Nutr 1998, V68(suppl), P1390S
(12) Aoyama, T; Biosci Biotechnol Biochem 2000, V64, P2594 HCAPLUS
(13) Aoyama, T; Nutrition 2000, V16, P349 HCAPLUS
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(15) Axelson, M; J Endocrinol 1984, V102, P49 HCAPLUS
(16) Baba, N; Nutr Res 1992, V12, P279 HCAPLUS
(17) Beguin, D; Poult Sci 1984, V63, P686 HCAPLUS
(18) Beynen, A; J Nutr 1990, V120, P422 HCAPLUS
(19) Bhathena, S; Fatty acids in foods and their health implications. 2nd ed 2000, P915 HCAPLUS
(20) Bierenbaum, M; Am Coll Nutr 1993, V12, P501 HCAPLUS
(21) Bosello, O; Ann Nutr Metab 1998, V32, P206
(22) Burant, C; J Clin Invest 1994, V93, P578 HCAPLUS
(23) Coward, L; J Agric Food Chem 1993, V41, P1961 HCAPLUS
(24) Crandall, D; Biochem Biophys Res Commun 1998, V248, P523 HCAPLUS
(25) Cunnane, S; Am J Clin Nutr 1995, V61, P62 MEDLINE
(26) Cunnane, S; Br J Nutr 1993, V69, P443 HCAPLUS
(27) Demonty, I; Lipids 1998, V33, P913 HCAPLUS
(28) FDA Food and Drug Administration; Fed Regist 1999, V64, P57700
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(30) Fisler, J; Int J Obes 1985, V9, P335 MEDLINE
(31) Forsythe, W; J Nutr 1986, V116, P1165 HCAPLUS
(32) Fort, P; J Am Coll Nutr 1986, V5, P439 MEDLINE
(33) Goodman-Gruen, D; J Nutr 2001, V131, P1202 HCAPLUS
(34) Haytowitz, D; Legumes and legume products 1986, P1
(35) Hermansen, K; Diabetes Care 2001, V24, P228 MEDLINE
(36) Hisatomi, M; Jpn J Pharmacol 1997, V74, P203 HCAPLUS
(37) Howe, J; Metabolism 1990, V39, P1246 HCAPLUS
(38) Huppertz, C; J Biol Chem 2001, V276, P2520
(39) Hurley, C; Can J Physiol Pharmacol 1998, V76, P1000 HCAPLUS
(40) Hurley, C; J Nutr Biochem 1995, V6, P540 HCAPLUS
(41) Ikeda, A; Ann Nutr Metab 1993, V37, P101 HCAPLUS
(42) Iritani, N; J Nutr 1997, V127, P1077 HCAPLUS
(43) Ishihara, K; Nutr Sci Soy Protein 1996, V17, P94 HCAPLUS
(44) Jenkins, D; Am J Clin Nutr 1999, V69, P395 HCAPLUS
(45) Jenkins, D; Atherosclerosis 1989, V78, P99 MEDLINE
(46) Jones, P; Biochem Soc Trans 1994, V22, P209S HCAPLUS
(47) Jurowska, J; Gastroenterology 1992, V102, P550
(48) Kagawa, K; Life Sci 1996, V58, P1745 HCAPLUS
(49) Kaminskas, A; Vopr Pitan 1992, V5-6, P13
(50) Kawano-Takahashi, Y; Int J Obes 1986, V10, P293 HCAPLUS
(51) King, R; Am J Clin Nutr 1998, V67, P867 HCAPLUS
(52) Kirkman, L; Nutr Cancer 1995, V24, P1 HCAPLUS

(53) Kuiper, G; Endocrinology 1998, V139, P4252 HCAPLUS
(54) Lang, V; Am J Clin Nutr 1998, V67, P1197 HCAPLUS
(55) Lang, V; Eur J Clin Nutr 1999, V53, P959 HCAPLUS
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L128 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:793344** HCAPLUS
DN **137:293979**
TI Use of lignans in health foods with antiinflammatory and anti-aging properties
IN Cassidy, Aedin; Green, Martin Richard; Richards, Mark; Tasker, Maria Catherine
PA Unilever N.V., Neth.; Unilever PLC; Hindustan Lever Ltd.
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A23L001-30
ICS A61K035-78; A61K007-48
CC 17-6 (Food and Feed Chemistry)
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002080702	A1	20021017	WO 2002-EP3585	20020330

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2001-303208 A 20010404
AB The invention provides the use of one or more health components selected from the group of lignans, in particular lignans derived from flaxseed, **enterolactone**, enterodiol and precursors thereof, in particular secoisolariciresinol and **matairesinol** in the prodn. of foods with antiinflammatory and/or anti-aging properties. Also provided is a method of administering such components to persons in need of the intake of an antiinflammatory and/or anti-aging component.
ST lignan food additive antiinflammatory antiaging
IT **Skin, disease**
(**aging**; use of lignans in health foods with antiinflammatory and anti-**aging** properties)
IT Health food
(bars; use of lignans in health foods with antiinflammatory and anti-aging properties)
IT Chocolate
(candy; use of lignans in health foods with antiinflammatory and anti-aging properties)
IT Candy
(chocolate; use of lignans in health foods with antiinflammatory and anti-aging properties)
IT Carbohydrates, biological studies
Gelatins, biological studies
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(food coatings; use of lignans in health foods with antiinflammatory and anti-aging properties)
IT Coating materials
(food; use of lignans in health foods with antiinflammatory and anti-aging properties)
IT Beverages
(health; use of lignans in health foods with antiinflammatory and

anti-aging properties)
IT Fibroblast
(human skin; use of lignans in health foods with antiinflammatory and anti-aging properties)
IT **Aging, animal**
(inhibitors of; use of lignans in health foods with antiinflammatory and anti-aging properties)
IT Flaxseed
(lignans; use of lignans in health foods with antiinflammatory and anti-aging properties)
IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(procollagens, type I; use of lignans in health foods with antiinflammatory and anti-aging properties)
IT Beverages
(sports; use of lignans in health foods with antiinflammatory and anti-aging properties)
IT Food
(spreads; use of lignans in health foods with antiinflammatory and anti-aging properties)
IT **Anti-inflammatory agents**
Bakery products
Breakfast cereal
Confectionery
Cream substitutes
Encapsulation
Food preservatives
Health food
Human
Ice cream
Mayonnaise
Salad dressings
Sauces (condiments)
Soups
(use of lignans in health foods with antiinflammatory and anti-aging properties)
IT Decorins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(use of lignans in health foods with antiinflammatory and anti-aging properties)
IT Lignans
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of lignans in health foods with antiinflammatory and anti-aging properties)
IT 9005-25-8, Starch, biological studies
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(food coatings; use of lignans in health foods with antiinflammatory and anti-aging properties)
IT 363-24-6, Prostaglandin E2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(use of lignans in health foods with antiinflammatory and anti-aging properties)
IT **580-72-3, Matairesinol** 29388-59-8, Secoisolariciresinol **78473-71-9, Enterolactone** 80226-00-2, Enterodiol
RL: FFD (Food or feed use); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(use of lignans in health foods with antiinflammatory and anti-aging properties)
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Chavali, S; US 5762935 A 1998

(2) Clark, W; US 5837256 A 1998 HCAPLUS
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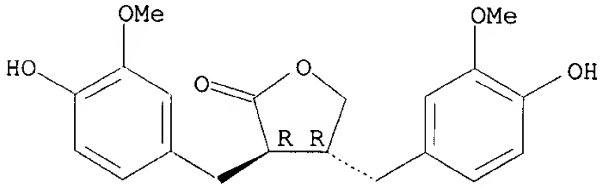
IT **580-72-3, Matairesinol 78473-71-9, Enterolactone**
RL: FFD (Food or feed use); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(use of lignans in health foods with antiinflammatory and anti-aging properties)

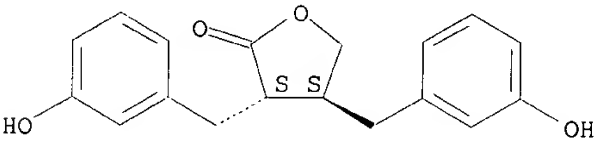
RN 580-72-3 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 78473-71-9 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L128 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:748794** HCAPLUS
DN **137:257656**
TI Use of two plant phenols in the treatment of arteriosclerosis
IN Rao, Janaswamy M.; Tiwari, Ashok K.; Srinivas, Pullela V.; Yadav, Jhillu S.; Raghavan, Kondapuram V.
PA Council of Scientific and Industrial Research, India
SO U.S., 7 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-365
NCL 514461000
CC 1-8 (Pharmacology)
Section cross-reference(s): 11, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6458831	B1	20021001	US 2000-698060	20001030
PRAI	US 2000-698060		20001030		

AB This invention relates to the isolation of two compds. namely (-)-**matairesinol** and (-)-wikstromol. These together with or assocd.

with therapeutically acceptable additives are useful as antioxidants and as free radical scavengers. The isolation of (-)-**matairesinol** and (-)-wikstromol from Cedrus deodara is described.

ST plant phenol Cedrus arteriosclerosis treatment

IT Drug delivery systems
(additives; use of two plant phenols from Cedrus deodara in treatment of arteriosclerosis in relation to free radical scavenger antioxidant activity)

IT Drug delivery systems
(oral; use of two plant phenols from Cedrus deodara in treatment of arteriosclerosis in relation to free radical scavenger antioxidant activity)

IT Carbohydrates, biological studies
Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical additives; use of two plant phenols from Cedrus deodara in treatment of arteriosclerosis in relation to free radical scavenger antioxidant activity)

IT **Antiarteriosclerotics**
Antioxidants
Arteriosclerosis
Cedrus deodara
Radical scavengers
(use of two plant phenols from Cedrus deodara in treatment of arteriosclerosis in relation to free radical scavenger antioxidant activity)

IT **580-72-3P**, (-)-**Matairesinol** 34444-37-6P, (-)-Wikstromol
RL: NPO (Natural product occurrence); **PAC (Pharmacological activity)**; PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); **USES (Uses)**
(use of two plant phenols from Cedrus deodara in treatment of arteriosclerosis in relation to free radical scavenger antioxidant activity)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

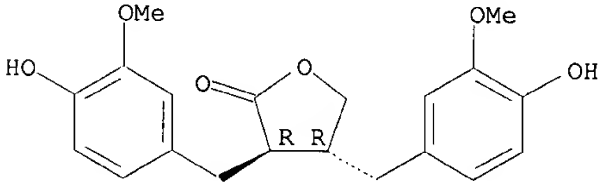
(1) Anon; JP 11180869 1999 HCAPLUS
(2) Anon; WO 0059946 2000 HCAPLUS
(3) Belletire; J Org Chem 1988, V53, P4724 HCAPLUS
(4) Maccrae; Biochemistry 1984, V23(6), P1207

IT **580-72-3P**, (-)-**Matairesinol**
RL: NPO (Natural product occurrence); **PAC (Pharmacological activity)**; PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); **USES (Uses)**
(use of two plant phenols from Cedrus deodara in treatment of arteriosclerosis in relation to free radical scavenger antioxidant activity)

RN 580-72-3 HCAPLUS

CN 2(3H)-Furanone, dihydro-3,4-bis[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L128 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:675761 HCAPLUS
DN 137:184820
TI Process for the fractionation of cereal brans
IN Kvist, Sten; Carlsson, Tommie; Lawther, John Mark; Basile de Castro, Fernando
PA Biovelop International B.V., Neth.
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A23L001-10
ICS A23J001-12
CC 17-11 (Food and Feed Chemistry)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002067698	A1	20020906	WO 2002-SE309	20020221
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	SE 2001000655	A	20020827	SE 2001-655	20010226
	SE 2001003328	A	20020827	SE 2001-3328	20011004
PRAI	SE 2001-655	A	20010226		
	SE 2001-3328	A	20011004		

AB A process for the fractionation of valuable fractions from cereal brans (e.g. wheat, barley and oat brans, and rice polish) is described. In particular, this invention describes a two step process, in which the said bran is first subjected to a combination of enzymic treatment and wet milling, followed by sequential centrifugation and ultrafiltration, which aims at phys. sepg. the main bran factions, i.e. insol. phase (pericarp and aleurone layer), germ-rich fraction, residual endosperm fraction and sol. sugars. A second step consists of fractionating cereal brans substantially free of sol. compds., hence insol. phase from the above-mentioned first step, by enzymic treatment with xylanase and/or beta-glucanase and wet milling, followed by sequential centrifugation and ultrafiltration, which aims at phys. sepg. the main fractions, i.e. insol. phase (remaining cell wall components), protein-rich fraction, sol. hemicellulose and oligosaccharide, and therefore maximizes the extn. rate of valuable cell wall components and aleurone cells from previously cleaned bran.
ST cereal bran fractionation xylanase glucanase milling centrifugation ultrafiltration
IT Bran
(barley; process for the fractionation of cereal brans)
IT Oat
Rice (Oryza sativa)
Triticale
(bran; process for the fractionation of cereal brans)
IT Enzymes, biological studies
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(cereal bran-degrading; process for the fractionation of cereal brans)
IT Fats and Glyceridic oils, biological studies
RL: FFD (Food or feed use); IMF (Industrial manufacture); BIOL (Biological

study); PREP (Preparation); USES (Uses)
(cereal germ; process for the fractionation of cereal brans)
IT Bran
(cereal; process for the fractionation of cereal brans)
IT Food functional properties
(emulsion stability; process for the fractionation of cereal brans)
IT Seed
(endosperm; process for the fractionation of cereal brans)
IT Proteins
RL: FFD (Food or feed use); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fat-binding; process for the fractionation of cereal brans)
IT Seed
Wheat
(germ; process for the fractionation of cereal brans)
IT Beverages
(health; process for the fractionation of cereal brans)
IT Beverages
(high protein; process for the fractionation of cereal brans)
IT Bran
(oat; process for the fractionation of cereal brans)
IT Plant tissue
(pericarp; process for the fractionation of cereal brans)
IT Sterols
RL: FFD (Food or feed use); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phyto-; process for the fractionation of cereal brans)
IT Aleurone
Anticholesteremic agents
Antitumor agents
Bakery products
Breakfast cereal
Cell wall
Centrifugation
Color
Dairy products
Dietary fiber
Drying apparatus
Evaporators
Feed additives
Food additives
Food emulsifying capacity
Food foaming
Food functional properties
Food preservation
Food solubility
Fractionation
Gelation agents
Health food
Meat
Meat substitutes
Sauces (condiments)
Soups
Syrups (sweetening agents)
Thickening agents
Ultrafiltration
Water binding (food)
Wheat bran
Whey
(process for the fractionation of cereal brans)
IT Phenols, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(process for the fractionation of cereal brans)

IT Fat substitutes
Glycolipids
Lecithins
Lignans
Monosaccharides
Phospholipids, biological studies
Protein hydrolyzates
RL: FFD (Food or feed use); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for the fractionation of cereal brans)

IT Carbohydrates, preparation
Oligosaccharides, preparation
Proteins
RL: IMF (Industrial manufacture); PREP (Preparation)
(process for the fractionation of cereal brans)

IT Bran
(rice; process for the fractionation of cereal brans)

IT Fats and Glyceridic oils, biological studies
RL: FFD (Food or feed use); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses)
(rye germ; process for the fractionation of cereal brans)

IT Bran
(rye; process for the fractionation of cereal brans)

IT Meat
(sausage; process for the fractionation of cereal brans)

IT Drying
(spray; process for the fractionation of cereal brans)

IT Bran
(triticale; process for the fractionation of cereal brans)

IT Milling (size reduction)
(wet; process for the fractionation of cereal brans)

IT Fats and Glyceridic oils, biological studies
RL: FFD (Food or feed use); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses)
(wheat germ; process for the fractionation of cereal brans)

IT 64-19-7, Acetic acid, biological studies 1135-24-6, Ferulic acid 1310-73-2, Sodium hydroxide, biological studies 7722-84-1, Hydrogen peroxide, biological studies 9000-92-4, Amylase 9001-92-7, Proteinase **9003-99-0, Peroxidase** 9032-08-0, Amyloglucosidase 9032-75-1, Pectinase 9068-42-2, Pentosanase 9074-98-0, .beta.-Glucanase 9075-53-0, Polysaccharidase 37278-89-0, Xylanase 37341-58-5, Phytase
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(process for the fractionation of cereal brans)

IT 69-79-4P, Maltose 1109-28-0P, Maltotriose 1406-18-4P, Vitamin E 9040-27-1P, Arabinoxylan 9041-22-9P, .beta.-Glucan **78473-71-9P, Enterolactone**
RL: FFD (Food or feed use); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); **USES (Uses)**
(process for the fractionation of cereal brans)

IT 9034-32-6P, Hemicellulose
RL: IMF (Industrial manufacture); PREP (Preparation)
(process for the fractionation of cereal brans)

IT 124-38-9, Carbon dioxide, biological studies
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(supercrit.; process for the fractionation of cereal brans)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

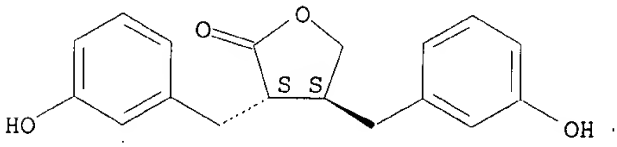
RE

(1) Chwalek; US 4171383 A 1979
(2) Chwalek; US 4171384 A 1979
(3) Gerrish; US 3879373 A 1975 HCAPLUS
(4) Keim; US 4361651 A 1982 HCAPLUS
(5) Konno; US 5308618 A 1994 HCAPLUS

(6) Myllymaki; US 5312636 A 1994
(7) Stone; US 4746073 A 1988
IT **9003-99-0, Peroxidase**
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(process for the fractionation of cereal brans)
RN 9003-99-0 HCAPLUS
CN Peroxidase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **78473-71-9P, Enterolactone**
RL: FFD (Food or feed use); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); **USES (Uses)**
(process for the fractionation of cereal brans)
RN 78473-71-9 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L128 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:332044** HCAPLUS
DN **136:319438**
TI Pharmaceutical composition comprising wikstromol and/or **matairesinol**, its use as hepatoprotectant and process for their isolation from Cedrus deodara
IN Rao, Janaswamy Madhusudana; Srinivas, Pullela Venkata; Yadav, Jhillu Singh; Raghavan, Kondapuram Vijaya
PA Council of Scientific and Industrial Research, India; Tiwari, Ashok, Kumar
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K035-78
ICS A61K031-365; A61P009-10; A61P001-16; A61K031-365; A61K031-365
CC 1-12 (Pharmacology)
Section cross-reference(s): 11, 63
FAN.CNT 1

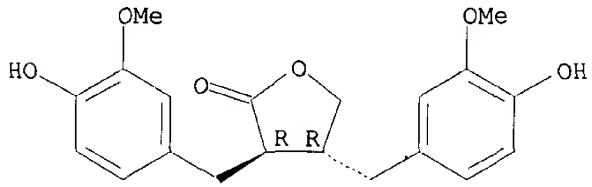
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002034277	A1	20020502	WO 2000-IN104	20001023
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001035969	A5	20020506	AU 2001-35969	20001023
PRAI	WO 2000-IN104	A	20001023		

AB This invention relates to the isolation of two compds. namely (-)-**matairesinol** and (-)-wikstromol together with or assocd. with a therapeutically acceptable additives and useful as an antioxidants and hepatoprotective agents.

ST **matairesinol** wikstromol hepatoprotectant isolation Cedrus
IT Drug delivery systems
(additives; pharmaceutical compn. comprising wikstromol and/or **matairesinol** and their use as antioxidants and hepatoprotectant and process for isolation from Cedrus deodara)
IT **Antiarteriosclerotics**
(antiatherosclerotics; pharmaceutical compn. comprising wikstromol and/or **matairesinol** and their use as antioxidants and hepatoprotectant and process for isolation from Cedrus deodara)
IT Drug delivery systems
(carriers; pharmaceutical compn. comprising wikstromol and/or **matairesinol** and their use as antioxidants and hepatoprotectant and process for isolation from Cedrus deodara)
IT Cytoprotective agents
(hepatoprotectants; pharmaceutical compn. comprising wikstromol and/or **matairesinol** and their use as antioxidants and hepatoprotectant and process for isolation from Cedrus deodara)
IT Carbohydrates, biological studies
Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in drug formulation; pharmaceutical compn. comprising wikstromol and/or **matairesinol** and their use as antioxidants and hepatoprotectant and process for isolation from Cedrus deodara)
IT Drug delivery systems
(oral; pharmaceutical compn. comprising wikstromol and/or **matairesinol** and their use as antioxidants and hepatoprotectant and process for isolation from Cedrus deodara)
IT Antioxidants
Cedrus deodara
Radical scavengers
(pharmaceutical compn. comprising wikstromol and/or **matairesinol** and their use as antioxidants and hepatoprotectant and process for isolation from Cedrus deodara)
IT 67-66-3, Chloroform, uses 110-54-3, Hexane, uses
RL: NUU (Other use, unclassified); USES (Uses)
(as solvent in drug isolation; pharmaceutical compn. comprising wikstromol and/or **matairesinol** and their use as antioxidants and hepatoprotectant and process for isolation from Cedrus deodara)
IT 67-56-1, Methanol, uses 141-78-6, Ethyl acetate, uses
RL: NUU (Other use, unclassified); USES (Uses)
(in drug isolation; pharmaceutical compn. comprising wikstromol and/or **matairesinol** and their use as antioxidants and hepatoprotectant and process for isolation from Cedrus deodara)
IT **580-72-3P**, (-)-**Matairesinol** 34444-37-6P, (-)-Wikstromol
RL: NPO (Natural product occurrence); **PAC (Pharmacological activity)**; PRP (Properties); PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); **USES (Uses)**
(pharmaceutical compn. comprising wikstromol and/or **matairesinol** and their use as antioxidants and hepatoprotectant and process for isolation from Cedrus deodara)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Archer Daniels Midland Co; EP 0906761 A 1999 HCAPLUS
(2) Inst Biolog Morya Dalnevostoch; GB 2198041 A 1988 HCAPLUS
(3) Umezawa, T; MOKUZAI GAKKAISHI 1996, V42(2), P180 HCAPLUS
IT **580-72-3P**, (-)-**Matairesinol**
RL: NPO (Natural product occurrence); **PAC (Pharmacological activity)**; PRP (Properties); PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); **USES (Uses)**
(pharmaceutical compn. comprising wikstromol and/or

matairesinol and their use as antioxidants and hepatoprotectant and process for isolation from Cedrus deodara)
RN 580-72-3 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L128 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:293387 HCAPLUS
DN 136:314998
TI Compositions for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase
IN Kragie, Laura
PA USA
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002030355	A2	20020418	WO 2001-US32066	20011010
	WO 2002030355	A3	20030206		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002013198	A5	20020422	AU 2002-13198	20011010
PRAI	US 2000-239457P	P	20001011		
	WO 2001-US32066	W	20011010		

AB This disclosure describes compns. and methods of use of compns., that can replace the role of estrogens in the functions of humans and other animals, when these humans or animals are under the influence of compds., devices and biologicals that can inhibit the activity of aromatase enzyme (estrogen synthetase). The estrogen function replacement agent is chosen from the group consisting of (i) prodrugs that are metabolized into an active agent in vivo by such enzymes reactions as hydrolysis, dehydroxylation, etc., (ii) a caged-precursor, a chem. structure that undergoes transformation when triggered by a stimulus such as light or bioelec. activity; a compd. produced de novo in a protected compartment implanted within the human or animal; and a full estrogen receptor agonist such as estradiol.
ST aromatase inhibitor estrogen function
IT Drug delivery systems
(aerosols, inhalants; compns. for alleviating adverse side effects

and/or enhancing efficacy of agents inhibiting aromatase)
IT **Skin, disease**
(**aging**; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Estrogens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiestrogens; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Polycyclic compounds
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(arom. hydrocarbons; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(beads, latex; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT **Transplant and Transplantation**
(bone marrow; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(buccal; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Candida
(candidiasis from, esophageal; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(caplets; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(capsules, soft; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(capsules; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Tobacco products
(cigarettes; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT **Acne**
Alopecia
Bacteria (Eubacteria)
Bark
Biosensors
Candy
Cereal (grain)
Chewing gum
Contraceptives
DNA sequences
Embryophyta
Flower
Food
Fruit
Fungicides
Headache
Hirsutism
Human
Hydrolysis
Hyperplasia
Hypertension
Immunodeficiency
Leaf

Organelle
Osteoporosis
Perfumes
Plasmids
Pregnancy
Psychotropics
Soups
Spices
Thrombosis
Tobacco smoke
Vaccines
Vegetable
Virus
(compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Antibodies
Flavonoids
Gelatins, biological studies
Glycoproteins
Hormones, animal, biological studies
Lipids, biological studies
Nucleic acids
Nucleoproteins
Oligonucleotides
Peptides, biological studies
Pheromones, animal
Polymers, biological studies
Proteins
Soaps
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Nervous system
(degeneration; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Drug delivery systems
(depot; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Cardiovascular system
(disease; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Parturition
(dysfunctional; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Drug delivery systems
(elixirs; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Drug delivery systems
(emulsions; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Gene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(expression, recombinant; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Smoke
(exts.; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Heart, disease
(failure; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Estrogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(function replacement; compns. for alleviating adverse side effects

and/or enhancing efficacy of agents inhibiting aromatase)
IT **Meningitis**
(fungal; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(gels; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(granules; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Candy
(hard; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Reproductive tract
(hypogonadism; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(immediate-release; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(implants; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Vagina
(infection; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(infusion pumps; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Medical goods
(inhalers; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(injections, i.m.; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(injections, i.v.; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(injections, s.c.; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Tobacco
(leaves; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(liposomes; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(lotions; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(lozenges; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Fertility
(male, disorder; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(microparticles; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(microspheres; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Headache
(migraine; compns. for alleviating adverse side effects and/or

enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(mucosal; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Mammary gland
Prostate gland
(neoplasm; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(ointments, creams; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(ointments; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(ophthalmic; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(oral; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(osmotic pumps; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(parenterals; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Blood vessel, disease
(peripheral; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Estrogens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phytoestrogens; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Aromatic hydrocarbons, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polycyclic; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(powders, inhalants; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(powders; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(prodrugs; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(rectal; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(solns.; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Cell
(stem; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Drug delivery systems
(sublingual; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Diet
(supplements; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
IT Vitamins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(supplements; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Drug delivery systems
(suppositories; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Drug delivery systems
(suspensions; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Drug delivery systems
(sustained-release; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Drug delivery systems
(tablets, chewable; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Drug delivery systems
(tablets, effervescent; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Drug delivery systems
(tablets; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Beverages
Tea (Camellia sinensis)
(tobacco-derived; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Drug delivery systems
(topical; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Drug delivery systems
(transdermal; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT Bone marrow
(transplant; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT 50-28-2, Estradiol, biological studies 50-29-3, DDT, biological studies 53-16-7, Estrone, biological studies 68-22-4, Norethisterone 80-05-7, Bisphenol A, biological studies 92-52-4D, 1,1'-Biphenyl, chloro derivs. 112-80-1, Oleic acid, biological studies 125-84-8, Aminoglutethimide 446-72-0, Genistein 480-40-0, Chrysin 486-66-8, Daidzein 491-80-5, Genistein 4'-methyl ether 566-48-3, 4-Hydroxyandrostenedione 604-59-1, .alpha.-Naphthoflavone 4416-57-3, Testololactone 10540-29-1, Tamoxifen 22916-47-8, Miconazole 23593-75-1, Clotrimazole 25265-71-8, Dipropylene glycol 27220-47-9, Econazole 27523-40-6, Isoconazole 35212-22-7, Ipriflavone 42959-18-2, Teas 59467-70-8, Midazolam 60628-96-8, Bifonazole 65277-42-1, Ketoconazole 65899-73-2, Tioconazole **78473-71-9, Enterolactone** 84449-90-1, Raloxifene 92788-10-8, Rogletimide 96301-34-7, Atamestane 97322-87-7, Troglitazone 102676-47-1, Fadrozole 107868-30-4, Exemestane 112809-51-5, Letrozole 120051-39-0, NKS 01 120511-73-1, Arimidex 129731-10-8, Vorozole 137234-62-9, Voriconazole 148869-05-0, YM-511
RL: **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

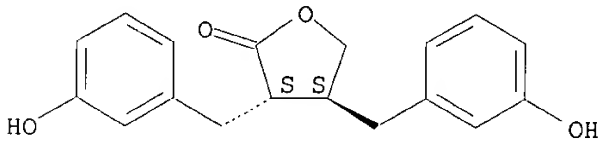
IT 9039-48-9, Aromatase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sensitizer; compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)

IT **78473-71-9, Enterolactone**

RL: **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(compns. for alleviating adverse side effects and/or enhancing efficacy of agents inhibiting aromatase)
RN 78473-71-9 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L128 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:122407 HCAPLUS
DN 136:384375
TI Association between low serum **enterolactone** and increased plasma F2-isoprostanes, a measure of lipid peroxidation
AU Vanharanta, Meri; Voutilainen, Sari; Nurmi, Tarja; Kaikkonen, Jari; Roberts, L. Jackson; Morrow, Jason D.; Adlercreutz, Herman; Salonen, Jukka T.
CS Research Institute of Public Health, University of Kuopio, Kuopio, 70211, Finland
SO Atherosclerosis (Shannon, Ireland) (2002), 160(2), 465-469
CODEN: ATHSBL; ISSN: 0021-9150
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
CC 14-15 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
AB Evidence suggests that low serum **enterolactone** concn. might be an independent risk factor for acute coronary events. **Enterolactone** is a lignan, which is formed by intestinal bacteria from precursors in plant foods. Due to the biphenolic structure of **enterolactone**, it could act as an antioxidant and through this contribute to cardiovascular health. The aim of this study was to test the hypothesis that a low serum **enterolactone** concn. is assocd. with increased in vivo lipid peroxidn., assessed by plasma F2-isoprostane concns. We investigated this assocn. in a subset of participants in 'The Antioxidant Supplementation in Atherosclerosis Prevention' (ASAP) study. Out of 256 male participants a subsample of 100 consecutive men from baseline was selected for F2-isoprostane assays. The mean serum **enterolactone** concn. was 16.6 nmol/l and that of F2-isoprostanes 29.6 ng/l. The correlation coeff. for assocn. between serum **enterolactone** and F2-isoprostane concns. was -0.30 ($P<0.003$). Plasma F2-isoprostane levels decreased linearly across quintiles of serum **enterolactone** concn. ($P=0.008$ for a linear trend). In a multivariate model, **enterolactone** persisted as a significant predictor after adjustment for vitamins and other variables, with the strongest assocns. with F2-isoprostanes. Our present data suggest that low serum **enterolactone** concn. is assocd. with enhanced in vivo lipid peroxidn. in men.
ST F2isoprostane hypercholesterolemia prognosis heart disease; **enterolactone** lipid peroxidn cancer
IT Blood serum
Human
Hypercholesterolemia
Neoplasm

Prognosis
Risk assessment
Sex
(altered serum **enterolactone** and F2-isoprostanes in assocn. with enhanced lipid peroxidn. and as prognostic factors for cardiovascular diseases and cancers in men with moderate hypercholesterolemia)

IT Cardiovascular system
(disease; altered serum **enterolactone** and F2-isoprostanes in assocn. with enhanced lipid peroxidn. and as prognostic factors for cardiovascular diseases and cancers in men with moderate hypercholesterolemia)

IT Prostaglandins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(prostanoids, F2-isoprostanes; altered serum **enterolactone** and F2-isoprostanes in assocn. with enhanced lipid peroxidn. and as prognostic factors for cardiovascular diseases and cancers in men with moderate hypercholesterolemia)

IT **78473-71-9, Enterolactone**
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); **USES (Uses)**
(altered serum **enterolactone** and F2-isoprostanes in assocn. with enhanced lipid peroxidn. and as prognostic factors for cardiovascular diseases and cancers in men with moderate hypercholesterolemia)

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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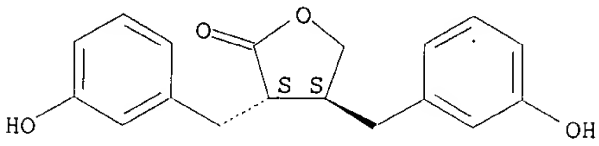
IT **78473-71-9, Enterolactone**
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); **USES (Uses)**
(altered serum **enterolactone** and F2-isoprostanes in assocn. with enhanced lipid peroxidn. and as prognostic factors for cardiovascular diseases and cancers in men with moderate

hypercholesterolemia)
RN 78473-71-9 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



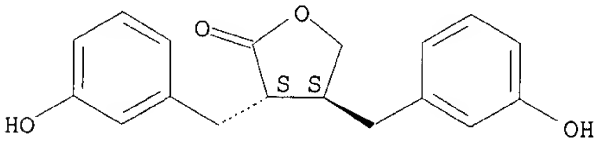
L128 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:51256** HCAPLUS
DN **136:107532**
TI Combinations of statins, estrogenic agents and optionally estrogens
IN Jenkins, Simon Nicholas; Komm, Barry Samuel; Miller, Christopher Paul
PA American Home Products Corporation, USA
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002003977	A2	20020117	WO 2001-US21085	20010629
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002019391	A1	20020214	US 2001-896353	20010629
	US 6465454	B2	20021015		
	US 2002025952	A1	20020228	US 2001-896632	20010629
PRAI	US 2000-216096P	P	20000706		
	US 2000-216184P	P	20000706		

OS MARPAT 136:107532
AB This invention comprises methods of treating cardiovascular disorders and lowering blood LDL levels comprising administration of a statin, an estrogen and indole derivs. Thus, a rapid dissoln. formulation contained micronized TSE-424 acetate 10.00, Lactose NF fast flow 33.10, Avicel PH-101 25.00, Starch-1500 20.00, sodium lauryl sulfate 1.50, sodium starch glycolate 10.00, Syloid-244 FP 0.15, and Mg stearate 0.25%.
ST estrogen statin cardiovascular disorder; indole deriv estrogen cardiovascular disorder; anticholesteremic estrogen statin
IT **Anticholesteremic agents**
Cardiovascular agents
(combinations of statins, estrogenic agents and optionally estrogens)
IT Estrogens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of statins, estrogenic agents and optionally estrogens)
IT Estrogens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugated; combinations of statins, estrogenic agents and optionally

estrogens)
IT Artery, disease
(coronary; combinations of statins, estrogenic agents and optionally estrogens)
IT Cardiovascular system
(disease; combinations of statins, estrogenic agents and optionally estrogens)
IT Drug delivery systems
(granules; combinations of statins, estrogenic agents and optionally estrogens)
IT Drug delivery systems
(tablets; combinations of statins, estrogenic agents and optionally estrogens)
IT 198480-55-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ERA-923; combinations of statins, estrogenic agents and optionally estrogens)
IT 50-27-1, Estriol 50-28-2, 17.beta.-Estradiol, biological studies 53-16-7, Estrone, biological studies 57-63-6, Ethinylestradiol 72-33-3, Mestranol 474-86-2, Equilin 517-09-9, Equilenin 531-95-3, Equol 651-55-8, 17.alpha.-Dihydroequilin 1423-97-8, 17.beta.-Dihydroequilenin 6639-99-2, 17.alpha.-Dihydroequilenin 75330-75-5, Lovastatin **78473-71-9, Enterolactone** 79902-63-9, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 143201-11-0 198481-32-2 198481-33-3 389125-71-7 389131-04-8, Estradiene
RL: **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(combinations of statins, estrogenic agents and optionally estrogens)
IT **78473-71-9, Enterolactone**
RL: **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(combinations of statins, estrogenic agents and optionally estrogens)
RN 78473-71-9 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L128 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:51255 HCAPLUS
DN 136:107531
TI Combinations of bisphosphonates, estrogenic agents and optionally estrogens
IN Jenkins, Simon Nicholas; Komm, Barry Samuel; Miller, Christopher Paul
PA American Home Products Corporation, USA
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 2002003976	A2	20020117	WO 2001-US20970	20010629
	WO 2002003976	A3	20030103		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002019373	A1	20020214	US 2001-896154	20010629
	US 2002028792	A1	20020307	US 2001-896219	20010629
	EP 1299093	A2	20030409	EP 2001-952365	20010629
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2000-216069P	P	20000706		
	US 2000-216188P	P	20000706		
	WO 2001-US20970	W	20010629		

OS MARPAT 136:107531

AB Methods of treating bone disorders and lowering blood LDL levels comprise administration of a bisphosphonate, and an indole deriv. Thus, a rapid dissoln. formulation contained micronized TSE-424 acetate 10.00, Lactose-NF fast flow 33.10, Avicel-PH 101 25.00, Starch-1500 20.00, sodium lauryl sulfate 1.50, sodium starch glycolate 10.00, Syloid-244 FP 0.15, and Mg stearate 0.25%.

ST bone disorder bisphosphonate indole; estrogenic agent bisphosphonate anticholesteremic; estrogen bisphosphonate anticholesteremic

IT Bone, disease
(Paget's, inhibitors; combinations of bisphosphonates and estrogenic agents and optionally estrogens)

IT Antitumor agents
(bone, metastasis; combinations of bisphosphonates and estrogenic agents and optionally estrogens)

IT **Anticholesteremic agents**
Bone, disease
Granulation
(combinations of bisphosphonates and estrogenic agents and optionally estrogens)

IT Estrogens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of bisphosphonates and estrogenic agents and optionally estrogens)

IT Estrogens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugated; combinations of bisphosphonates and estrogenic agents and optionally estrogens)

IT Drug delivery systems
(granules; combinations of bisphosphonates and estrogenic agents and optionally estrogens)

IT Bone, neoplasm
(metastasis, inhibitors; combinations of bisphosphonates and estrogenic agents and optionally estrogens)

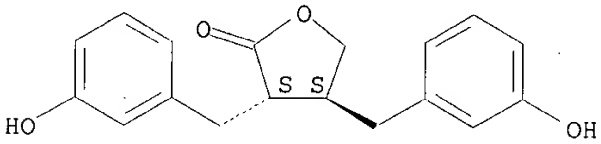
IT Bone, disease
(osteolysis, inhibitors; combinations of bisphosphonates and estrogenic agents and optionally estrogens)

IT Drug delivery systems
(tablets; combinations of bisphosphonates and estrogenic agents and optionally estrogens)

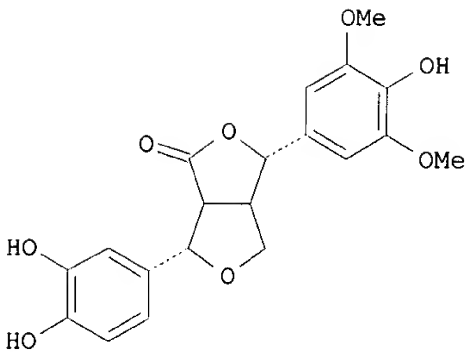
IT Osteoporosis
(therapeutic agents; combinations of bisphosphonates and estrogenic agents and optionally estrogens)

IT 389125-71-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ERA-923 hydrochloride monohydrate; combinations of bisphosphonates and estrogenic agents and optionally estrogens)
IT 198480-55-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ERA-923; combinations of bisphosphonates and estrogenic agents and optionally estrogens)
IT 50-27-1, Estriol 50-28-2, 17.beta.-Estradiol, biological studies 53-16-7, Estrone, biological studies 57-63-6, Ethinylestradiol 72-33-3, Mestranol 474-86-2, Equilin 517-09-9, Equilenin 531-95-3, Equol 651-55-8, 17.alpha.-DihydroEquilin 1423-97-8, 17.beta.-DihydroEquilenin 2809-21-4 3563-27-7, 17.beta.-DihydroEquilin 6639-99-2, 17.alpha.-DihydroEquilenin 10596-23-3 13598-36-2D, Phosphonic acid, alkylidenebis- derivs. 40391-99-9 66376-36-1, Alendronate **78473-71-9**, **Enterolactone** 79778-41-9, Neridronate 89987-06-4, Tiludronate 105462-24-6 114084-78-5, Ibandronate 118072-93-8, Zoledronate 121368-58-9, Olpadronate 138330-18-4, Incadronate 180064-38-4 198481-32-2 198481-33-3 389131-04-8, Estradiene
RL: **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(combinations of bisphosphonates and estrogenic agents and optionally estrogens)
IT **78473-71-9**, **Enterolactone**
RL: **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(combinations of bisphosphonates and estrogenic agents and optionally estrogens)
RN 78473-71-9 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L128 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:922174 HCAPLUS
DN 136:291701
TI Immunosuppressive constituents from Saussurea medusa
AU Duan, Hongquan; Takaishi, Yoshihisa; Momota, Hiroshi; Ohmoto, Yasukazu; Taki, Takao
CS Faculty of Pharmaceutical Sciences, University of Tokushima, Tokushima, 770-8505, Japan
SO Phytochemistry (2002), 59(1), 85-90
CODEN: PYTCAS; ISSN: 0031-9422
PB Elsevier Science Ltd.
DT Journal
LA English
CC 11-1 (Plant Biochemistry)
Section cross-reference(s): 26
GI



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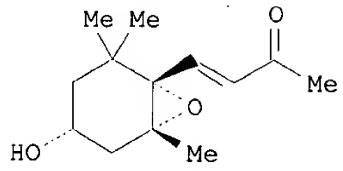


II

AB The methanol ext. of Saussurea medusa Maxim afforded two lignans: (e.g. I) and 1-hydroxy-2,4-guaicyl-3,7-dioxabicyclo[3.3.0]octane; two chlorophyll derivs.: 13-epi-phaeophorbide-a and 13-epi-phaeophorbide-a Me ester; one megastigmane deriv.: 3-hydroxy-5,6-epoxy-7-megastigmen-9-one (II), along with 19 known compds. Their structures were established on the basis of spectroscopic studies.

ST lignan chlorophyll megastigmane deriv Saussurea immunosuppressant

IT Chlorophylls, biological studies
RL: BSU (Biological study, unclassified); NPO (Natural product occurrence); PAC (Pharmacological activity); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(derivs.; immunosuppressive constituents from Saussurea medusa)

IT **Immunosuppressants**
Saussurea medusa
(immunosuppressive constituents from Saussurea medusa)

IT Lignans
RL: BSU (Biological study, unclassified); NPO (Natural product occurrence); PAC (Pharmacological activity); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(immunosuppressive constituents from Saussurea medusa)

IT Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition effect on cytokinins of immunosuppressive constituents from Saussurea medusa)

IT New natural products
(lignans, chlorophyll derivs. and megastigmane deriv. from Saussurea medusa)

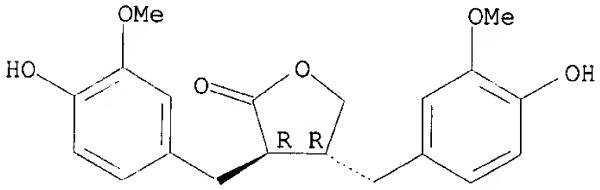
IT Molecular structure, natural product
(of lignans, chlorophyll derivs. and megastigmane deriv. from Saussurea medusa)

IT 64070-09-3P, 13-epi-Phaeophorbide-a methyl ester 78964-31-5P, 13-epi-Phaeophorbide-a 175418-93-6P 408513-60-0P 408513-62-2P, 1.alpha.-Hydroxy-2.alpha.,4.alpha.-guaicyl-3,7-dioxabicyclo[3.3.0]octane
RL: BSU (Biological study, unclassified); NPO (Natural product occurrence); PAC (Pharmacological activity); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(immunosuppressive constituents from Saussurea medusa)

IT 487-36-5, (+)-Pinoresinol **580-72-3, Matairesinol**

603-17-8, Pheophytin a 3147-18-0, Pheophytin b 5594-30-9, Methyl phaeophoride a 5989-02-6, Loliolide 6216-81-5, Lirioresinol B 7770-78-7, Arctigenin 15664-29-6, Phaeophorbide a 20240-17-9 20362-31-6, Arctiin 24404-50-0, Epipinoresinol 27003-73-2, Lariciresinol 29388-59-8, Secoisolariciresinol 40957-99-1, (+)-Medioresinol 79733-01-0 79733-03-2 99305-01-8 126882-59-5, (-)-Berchemol
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; BIOL (Biological study)
(immunosuppressive constituents from Saussurea medusa)
IT 408512-16-3P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and properties of)
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Briggs, L; Journal of Chemical Society (C) 1968, P3042 HCAPLUS
(2) Chan, Y; Chemical and Pharmaceutical Bulletin 1999, V47, P887 HCAPLUS
(3) Duan, H; Phytochemistry 2000, V53, P805 HCAPLUS
(4) Fang, J; Phytochemistry 1989, V28, P3553 HCAPLUS
(5) Fonseca, S; Phytochemistry 1978, V17, P499
(6) Hodges, R; Tetrahedron 1964, V20, P1463 HCAPLUS
(7) Kita, M; Microbiology and Immunology 1992, V36, P507 HCAPLUS
(8) Kobayashi, M; Chemical and Pharmaceutical Bulletin 1991, V39, P3348 HCAPLUS
(9) Li, Y; Phytochemistry 1989, V28, P3395 HCAPLUS
(10) Nakatani, Y; Chemical and Pharmaceutical Bulletin 1981, V29, P2261 HCAPLUS
(11) Rahman, M; Phytochemistry 1990, V29, P1971 HCAPLUS
(12) Sakurai, N; Chemical and Pharmaceutical Bulletin 1989, V37, P3311 HCAPLUS
(13) Takeda, Y; Phytochemistry 1997, V44, P1335 HCAPLUS
(14) Tsukamoto, H; Chemical and Pharmaceutical Bulletin 1984, V32, P4482 HCAPLUS
(15) Wray, V; Tetrahedron 1979, V35, P2275 HCAPLUS
(16) Yang, R; Natural Medicines 1997, V51, P134
IT **580-72-3, Matairesinol**
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; BIOL (Biological study)
(immunosuppressive constituents from Saussurea medusa)
RN 580-72-3 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L128 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:850871 HCAPLUS
DN 135:357106
TI Bakery products containing large amounts of oilseeds with phytoestrogens
IN Garai, Janos; Krausz, Erika
PA Hung.
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A21D002-36

ICS A21D002-26; A21D013-02; A21D013-04
CC 17-11 (Food and Feed Chemistry)
Section cross-reference(s): 1, 2, 18
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001087075	A1	20011122	WO 2001-HU32	20010321

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI HU 2000-1193 A 20000321

AB Crushed or milled oilseeds are incorporated into bakery products and used for suppression of the symptoms of menopause. Thus, 420 g linseed, 560 g soybeans, 100 g sesame seeds, and 150 g oats are combined with binders (550 g sugar, 150 g margarine, 1 egg, 0.1 L milk, 150 g wheat flour) and seasonings and flavorings into a sweet cake.

ST oilseed bakery product estrogen menopause

IT **Anticholesteremic agents**
Antioxidants
Antitumor agents
Appetite depressants
Butter
Digestion, biological
Egg, poultry
Flavor
Flavoring materials
Flaxseed
Flours and Meals
Hypolipemic agents
Menopause
Milling (size reduction)
Oat
Sesame (Sesamum indicum)
Soybean (Glycine max)
Wheat flour
(bakery products contg. large amts. of oilseeds with phytoestrogens)

IT Carbohydrates, biological studies
Shortening
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(bakery products contg. large amts. of oilseeds with phytoestrogens)

IT Bakery products
(cakes; bakery products contg. large amts. of oilseeds with phytoestrogens)

IT Bakery products
(cookies; bakery products contg. large amts. of oilseeds with phytoestrogens)

IT Bakery products
(crackers; bakery products contg. large amts. of oilseeds with phytoestrogens)

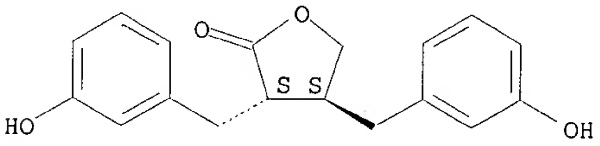
IT Bakery products
(oilseed-rich bakery products contg. phytoestrogens)

IT Seed
(oilseed; bakery products contg. large amts. of oilseeds with phytoestrogens)

IT Estrogens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); OCCU

(Occurrence); USES (Uses)
(phytoestrogens; bakery products contg. large amts. of oilseeds with phytoestrogens)
IT Bakery products
(pies, crusts; bakery products contg. large amts. of oilseeds with phytoestrogens)
IT 446-72-0, Genistein 486-66-8, Daidzein **78473-71-9, Enterolactone**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); FFD (Food or feed use); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); **USES (Uses)**
(plasma; bakery products contg. large amts. of oilseeds with phytoestrogens)
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; PATENT ABSTRACTS OF JAPAN 2000, V2000(06)
(2) Bahlsens, K; DE 3704715 A 1988
(3) Biasi, C; FR 2464028 A 1981
(4) Fuji Oil Co Ltd; JP 2000083572 A 2000 HCAPLUS
(5) Guenther, H; DE 19524041 A 1997
(6) Novopan Studiengesellschaft M; GB 388319 A 1933 HCAPLUS
(7) Riaz; CEREAL FOODS WORLD 1999, V44(2), P88
(8) Riegler, H; DE 3013003 A 1981
(9) Riegler, H; DE 4024222 A 1992
(10) Takemori, T; US 5026568 A 1991
(11) Unilever Nv; WO 9504462 A 1995 HCAPLUS
IT **78473-71-9, Enterolactone**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); FFD (Food or feed use); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); **USES (Uses)**
(plasma; bakery products contg. large amts. of oilseeds with phytoestrogens)
RN 78473-71-9 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L128 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:450166** HCAPLUS
DN **135:189741**
TI Anti-AIDS Agents. 46. Anti-HIV Activity of Harman, an Anti-HIV Principle from Symplocos setchuensis, and Its Derivatives
AU Ishida, Junko; Wang, Hui-Kang; Oyama, Masayoshi; Cosentino, Mark L.; Hu, Chang-Qi; Lee, Kuo-Hsiung
CS Natural Products Laboratory School of Pharmacy, University of North Carolina, Chapel Hill, NC, 27599-7360, USA
SO Journal of Natural Products (2001), 64(7), 958-960
CODEN: JNPRDF; ISSN: 0163-3864
PB American Chemical Society
DT Journal
LA English
CC 1-3 (Pharmacology)
Section cross-reference(s): 63
AB **Matairesinol** and harman, identified from Symplocos setchuensis,

were found to inhibit HIV replication in H9 lymphocyte cells. Anti-HIV evaluation of 28 derivs. of harman revealed that compd. 19 showed potent activity with EC50 and therapeutic index values of 0.037 .mu.M and 210, resp.

ST antiHIV Symplocos harman deriv SAR

IT **Lymphocyte**
(H9; anti-HIV principle from Symplocos setchuensis, and its derivs.)

IT **Anti-AIDS agents**
Structure-activity relationship
Symplocos
(anti-HIV principle from Symplocos setchuensis, and its derivs.)

IT 244-63-3, 9H-Pyrido[3,4-b]indole 442-51-3, Harmine 486-84-0, Harman 487-03-6 525-41-7 6028-07-5 6415-92-5 6519-18-2 10593-56-3, 9H-Pyrido[3,4-b]indole, 7-ethoxy-1-methyl- 17019-08-8 24415-61-0 85645-27-8 143502-37-8 186790-81-8 199530-62-6 199530-63-7 200431-10-3 241809-11-0 257938-75-3 257938-76-4 257938-77-5 257938-78-6 257938-79-7 257938-81-1 257938-82-2 257938-85-5 257938-86-6 356790-36-8 356790-37-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-HIV principle from Symplocos setchuensis, and its derivs.)

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
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L128 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2003 ACS

AN **2001:246421** HCAPLUS

DN **135:116810**

TI In vitro inhibitory effects of Daphne oleoides SSP. oleoides on inflammatory cytokines and activity-guided isolation of active constituents

AU Yesilada, Erdem; Taninaka, Hitomi; Takaishi, Yoshihisa; Honda, Gisho; Sezik, Ekrem; Momota, Hiroshi; Ohmoto, Yasukazu; Taki, Takao

CS Faculty of Pharmacy, Gazi University, Etiler, Ankara, 06330, Turk.

SO Cytokine (2001), 13(6), 359-364
CODEN: CYTIE9; ISSN: 1043-4666

PB Academic Press

DT Journal

LA English

CC 1-7 (Pharmacology)
Section cross-reference(s): 11

AB Aerial parts of Daphne oleoides Schreber ssp. oleoides (Thymelaeaceae) are used to treat rheumatoid arthritis and lumbago in Turkish folk medicine. In order to evaluate folkloric utilization, in vitro inhibitory effects of the Et acetate ext. and fractions obtained from this ext. on interleukin 1 (IL-1.alpha., IL-1.beta.) and **tumor necrosis factor (TNF-.alpha.)** biosynthesis were studied. Through chem. isolation techniques and activity-guided fractionation process, seventeen compds. were isolated and their structures were elucidated. Diterpenoids genkwadaphnin and 1,2-dehydrodaphnetoxin and a coumarin deriv. daphnetin showed potent inhibitory activity and were the main active ingredients. Furthermore,

gnidilatin, gnidilatin-20 palmitate, genkwadaphnin-20-palmitate and gnidicin-20-palmitate, having diterpenoid structure, and eudesmine, wikstromol and **matairesinol**, having lignan structure, were detd. to possess moderate inhibitory activity and may have a contributory role in the effect of the remedy. (c) 2001 Academic Press.

ST Daphne constituent inflammatory cytokine inhibitor

IT **Antirheumatic agents**
Daphne oleoides oleoides
(in vitro inhibitory effects of Daphne oleoides SSP. oleoides on inflammatory cytokines and activity-guided isolation of active constituents in relation to rheumatoid arthritis treatment)

IT Interleukin 1.alpha.
Interleukin 1.beta.
Tumor necrosis factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(in vitro inhibitory effects of Daphne oleoides SSP. oleoides on inflammatory cytokines and activity-guided isolation of active constituents in relation to rheumatoid arthritis treatment)

IT 93-35-6P, Umbelliferone 118-34-3P, Syringin 486-35-1P, Daphnetin 486-55-5P, Daphnin 508-02-1P, Oleanolic acid **580-72-3P**, **Matairesinol** 50432-89-8P 55073-32-0P, Genkwadaphnin 60195-67-7P, gnidilatin-20 palmitate 60195-69-9P, Gnidilatin 61521-74-2P, Wikstromol 124903-93-1P 260991-41-1P 260991-46-6P, Genkwadaphnin-20-palmitate 260991-48-8P, Gnidicin-20-palmitate 350819-97-5P 350819-98-6P
RL: **BAC (Biological activity or effector, except adverse)**; BOC (Biological occurrence); BSU (Biological study, unclassified); PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); **USES (Uses)**
(in vitro inhibitory effects of Daphne oleoides SSP. oleoides on inflammatory cytokines and activity-guided isolation of active constituents in relation to rheumatoid arthritis treatment)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
(1) Brennan, F; Lancet 1989, V2, P244 MEDLINE
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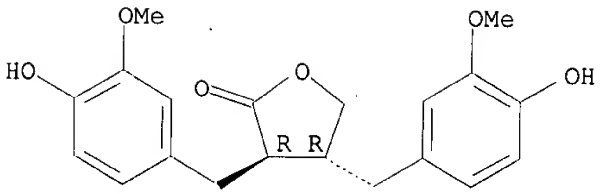
IT **580-72-3P, Matairesinol**
RL: **BAC (Biological activity or effector, except adverse)**; BOC (Biological occurrence); BSU (Biological study, unclassified); PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); **USES (Uses)**
(in vitro inhibitory effects of Daphne oleoides SSP. oleoides on inflammatory cytokines and activity-guided isolation of active constituents in relation to rheumatoid arthritis treatment)

RN 580-72-3 HCAPLUS

CN 2(3H)-Furanone, dihydro-3,4-bis[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L128 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:23769 HCAPLUS
DN 134:207205
TI Antioxidants in vegan diet and rheumatic disorders
AU Hanninen, O.; Kaartinen, K.; Rauma, A.-L.; Nenonen, M.; Torronen, R.; Hakkinen, S.; Adlercreutz, H.; Laakso, J.
CS Department of Physiology, University of Kuopio, Kuopio, 70211, Finland
SO Toxicology (2000), 155(1-3), 45-53
CODEN: TXCYAC; ISSN: 0300-483X
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
CC 18-7 (Animal Nutrition)
AB Plants are rich natural sources of antioxidants in addn. to other nutrients. Interventions and cross sectional studies on subjects consuming uncooked vegan diet called living food (LF) have been carried out. We have clarified the efficacy of LF in rheumatoid diseases as an example of a health problem where inflammation is one of the main concerns. LF is an uncooked vegan diet and consists of berries, fruits, vegetables and roots, nuts, germinated seeds and sprouts, i.e. rich sources of carotenoids, vitamins C and E. The subjects eating LF showed highly increased levels of beta and alfa carotenes, lycopene and lutein in their sera. Also the increases of vitamin C and vitamin E (adjusted to cholesterol) were statistically significant. As the berry intake was 3-fold compared to controls the intake of polyphenolic compds. like quercetin, myricetin and kaempferol was much higher than in the omnivorous controls. The LF diet is rich in fiber, substrate of lignan prodn., and the urinary excretion of polyphenols like enterodiol and **enterolactone** as well as secoisolariciresinol were much increased in subjects eating LF. The shift of fibromyalgic subjects to LF resulted in a decrease of their joint stiffness and pain as well as an improvement of their self-experienced health. The rheumatoid arthritis patients eating the LF diet also reported similar pos. responses and the objective measures supported this finding. The improvement of rheumatoid arthritis was significantly correlated with the day-to-day fluctuation of subjective symptoms. In conclusion the rheumatoid patients subjectively benefited from the vegan diet rich in antioxidants, lactobacilli and fiber, and this was also seen in objective measures.
ST antioxidant vegan diet rheumatoid arthritis
IT Antioxidants
Dietary fiber
Inflammation
Lactobacillus
Rheumatoid arthritis
(antioxidants in vegan diet and rheumatic disorders)
IT Carotenes, biological studies
Lignans
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antioxidants in vegan diet and rheumatic disorders)
IT Muscle, disease
(fibromyalgia; antioxidants in vegan diet and rheumatic disorders)

IT Diet
(vegetarian; antioxidants in vegan diet and rheumatic disorders)
IT 50-81-7, Vitamin c, biological studies 117-39-5, Quercetin 127-40-2, Lutein 502-65-8, Lycopene 520-18-3, Kaempherol 529-44-2, Myricetin 531-95-3, Equol **580-72-3**, **Matairesinol** 1406-18-4, Vitamin e 29388-59-8, Secoisolariciresinol **78473-71-9**, **Enterolactone** 80226-00-2, Enterodiol
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(antioxidants in vegan diet and rheumatic disorders)
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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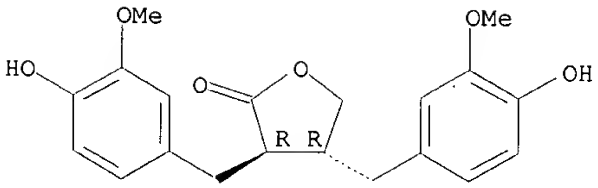
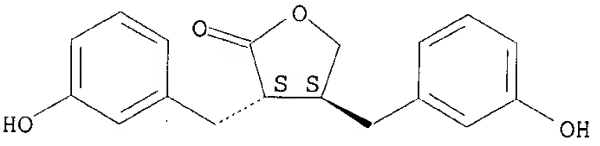
IT **580-72-3**, **Matairesinol** **78473-71-9**, **Enterolactone**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(antioxidants in vegan diet and rheumatic disorders)
RN 580-72-3 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 78473-71-9 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L128 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:241997 HCAPLUS
DN 130:287063
TI Method of preparing and using phytochemicals
IN Empie, Mark; Gugger, Eric
PA Archer Daniels Midland Company, USA
SO Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K035-78
ICS A23L001-30
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 14, 17, 18
FAN.CNT 5

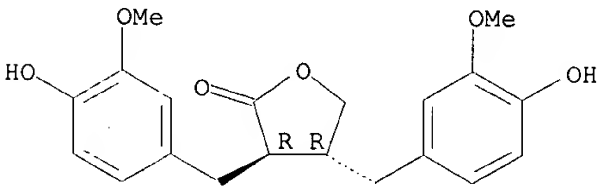
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 906761	A2	19990407	EP 1998-308060	19981002
	EP 906761	A3	19990519		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6261565	B1	20010717	US 1998-162038	19980928
	ZA 9808962	A	19990913	ZA 1998-8962	19981001
PRAI	US 1997-60549P	P	19971002		
	US 1998-162038	P	19980928		
	US 1996-614545	A3	19960313		
	US 1997-868629	A2	19970604		
	US 1998-35588	A2	19980305		

AB A compn. is prepd. by extg. phytochems. from plant matter. This compn. is enriched preferably in isoflavones, lignans, saponins, catechins and phenolic acids. Soy is the preferred source of these chems.; however, other plants may also be used, such as red clover, kudzu, flax, and cocoa. The compn. is a dietary supplement for treatment of various cancers, pre- and post-menstrual syndromes, and various other disorders.
ST phytochem prepn diet therapy; soybean phytochem prepn diet therapy
IT Animal cell line
(LNCaP; method of prepg. and dietary use of phytochems.)
IT Saponins
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological

study); USES (Uses)
(alfalfa; method of prepg. and dietary use of phytochems.)
IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood; method of prepg. and dietary use of phytochems.)
IT Drug delivery systems
(capsules; method of prepg. and dietary use of phytochems.)
IT Intestine, neoplasm
(colon; method of prepg. and dietary use of phytochems.)
IT Artery, disease
(coronary; method of prepg. and dietary use of phytochems.)
IT Mental disorder
(dementia; method of prepg. and dietary use of phytochems.)
IT Soybean (Glycine max)
(flour; method of prepg. and dietary use of phytochems.)
IT Flavones
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isoflavones; method of prepg. and dietary use of phytochems.)
IT Alfalfa (Medicago sativa)
Angiogenesis inhibitors
Antitumor agents
Apoptosis
Clover (Trifolium pratense)
Cocoa products
Diet
Drug delivery systems
Flax
Health food
Kudzu (Pueraria)
Nutrients
Proliferation inhibition
Skin, neoplasm
Soybean (Glycine max)
Tea (Camellia sinensis)
(method of prepg. and dietary use of phytochems.)
IT Flavanols
Ginsenosides
Lignans
Mineral elements, biological studies
Saponins
Vitamins
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of prepg. and dietary use of phytochems.)
IT Headache
(migraine; method of prepg. and dietary use of phytochems.)
IT Mammary gland
(neoplasm; method of prepg. and dietary use of phytochems.)
IT Carboxylic acids, biological studies
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(phenolic; method of prepg. and dietary use of phytochems.)
IT Chemicals
(phyto-; method of prepg. and dietary use of phytochems.)
IT Saponins
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soya; method of prepg. and dietary use of phytochems.)
IT Food
(soybean-based; method of prepg. and dietary use of phytochems.)
IT Flours and Meals
Molasses
Whey

(soybean; method of prepg. and dietary use of phytochems.)
IT Proteins, general, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soybean; method of prepg. and dietary use of phytochems.)
IT Drug delivery systems
(tablets; method of prepg. and dietary use of phytochems.)
IT Diet
(therapeutic; method of prepg. and dietary use of phytochems.)
IT 57-88-5, Cholest-5-en-3-ol (3.beta.)-, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(blood; method of prepg. and dietary use of phytochems.)
IT 50-70-4, Sorbitol, biological studies 63-42-3, Lactose 69-72-7, Salicylic acid, biological studies 121-34-6, Vanillic acid 149-91-7, Gallic acid, biological studies 154-23-4, Catechin, biological studies 156-38-7 327-97-9, Chlorogenic acid 331-39-5, Caffeic acid 446-72-0, Genistein 465-99-6, Hederagenin 485-72-3, Formononetin 486-66-8, Daidzein 487-36-5, Pinoresinol 490-46-0, Epicatechin 490-79-9, Gentisic acid 491-80-5, Biochanin A 500-38-9, Nordihydroguaiaretic acid 508-01-0, Soyasapogenol A 529-59-9, Genistin 530-57-4, Syringic acid 530-59-6, Sinapic acid 548-29-8, Isolariciresinol 552-66-9, Daidzin 557-04-0, Magnesium stearate **580-72-3, Matairesinol** 595-14-2, Soyasapogenol C 595-15-3, Soyasapogenol B 599-07-5, Medicagenic acid 621-82-9, Cinnamic acid, biological studies 970-73-0, Gallocatechin 970-74-1, Epigallocatechin 1135-24-6, Ferulic acid 1393-03-9 1405-86-3D, Glycyrrhizin, reaction with digitonin 2955-23-9, Olivil 6750-59-0, Soyasapogenol E 7440-70-2D, Calcium, compds., biological studies 7693-13-2, Calcium citrate 7757-93-9, Dicalcium phosphate 9004-34-6, Cellulose, biological studies 11024-24-1D, Digitonin, reaction with glycyrrhizin 17406-45-0, Tomatine 17482-42-7, Calcium malate 25429-38-3, Coumaric acid 27003-73-2, Lariciresinol 29388-59-8, Secoisolariciresinol 29656-58-4, Hydroxybenzoic acid 40957-83-3, Glycitein 56283-67-1, Lucernic acid 65892-76-4, Soyasapogenol D 84161-89-7, Zanhic acid 104033-83-2, Soyasapogenol F
RL: FFD (Food or feed use); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(method of prepg. and dietary use of phytochems.)
IT **78473-71-9, Enterolactone** 80226-00-2, Enterodiol
RL: FFD (Food or feed use); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(precursors; method of prepg. and dietary use of phytochems.)
IT **580-72-3, Matairesinol**
RL: FFD (Food or feed use); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(method of prepg. and dietary use of phytochems.)
RN 580-72-3 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)- (9CI) (CA INDEX NAME)

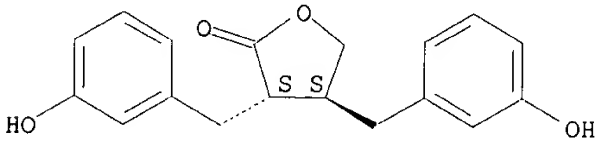
Absolute stereochemistry. Rotation (-).



IT **78473-71-9, Enterolactone**

RL: FFD (Food or feed use); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(precursors; method of prepg. and dietary use of phytochems.)
RN 78473-71-9 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L128 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN 1995:982949 HCAPLUS
DN 124:230
TI (-)-Arctigenin as a Lead Structure for Inhibitors of Human Immunodeficiency Virus Type-1 Integrase
AU Eich, Eckart; Pertz, Heinz; Kaloga, Macki; Schulz, Jutta; Fesen, Mark R.; Mazumder, Abhijit; Pommier, Yves
CS Institut fuer Pharmazeutische Biologie, Freie Universitaet Berlin, Berlin, D-14195, Germany
SO Journal of Medicinal Chemistry (1996), 39(1), 86-95
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
CC 1-3 (Pharmacology)
Section cross-reference(s): 26
AB The natural dibenzylbutyrolactone type lignanolide (-)-arctigenin (2), an inhibitor of human immunodeficiency virus type-1 (HIV-1) replication in infected human cell systems, was found to suppress the integration of proviral DNA into the cellular DNA genome.11b. In the present study 2 was tested with purified HIV-1 integrase and found to be inactive in the cleavage (3'-processing) and integration (strand transfer) step assays. However, a semisynthetic 3-O-demethylated congener characterized by a catechol substructure exhibited remarkable activities in both assays. Structure-activity relation studies with 30 natural , semisynthetic , and synthetic lignans revealed that (1) the lactone moiety is crucial since compds. with a butane-1,4-diol or THF substructure and also lignanamide analogs lacked activity and (2) the no. and arrangement of phenolic hydroxyl groups is important for the activity of lignanolides. A congener with two catechol substructures (7)was the most active compd. in this study. This compd. was also a potent inhibitor of the "disintegration' reaction which models the reversal of the strand transfer reaction. The inhibitory activity of 7 with the core enzyme fragment consisting of amino acids 50-212 suggests that the binding site of 7 resides in the catalytic domain.
ST arctigenin analog immunodeficiency virus integrase inhibitor
IT Molecular structure-biological activity relationship
Virucides and Virustats
((-)-arctigenin as a lead structure for inhibitors of human immunodeficiency virus type-1 integrase)
IT **Virus, animal**
(**human immunodeficiency 1**, (-)-arctigenin as a lead structure for inhibitors of human immunodeficiency virus type-1 integrase)
IT 518-29-6P, .beta.-Peltatin 568-53-6P, .alpha.-Peltatin **580-72-3P**, (-)-**Matairesinol** 7770-78-7P, (-)-Arctigenin 40505-27-9P

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); **USES (Uses)**
((-)-arctigenin as a lead structure for inhibitors of human immunodeficiency virus type-1 integrase)

IT 29388-33-8P 29388-59-8P 73354-08-2P 119069-38-4P 147022-95-5P 157072-28-1P 171260-18-7P 171260-36-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
((-)-arctigenin as a lead structure for inhibitors of human immunodeficiency virus type-1 integrase)

IT 477-46-3P 641-25-8P 105662-24-6P 112066-16-7P 119098-95-2P 144849-35-4P 171260-17-6P 171260-19-8P 171260-20-1P 171260-29-0P 171260-30-3P 171260-31-4P 171260-32-5P 171260-33-6P 171260-34-7P 171260-37-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
((-)-arctigenin as a lead structure for inhibitors of human immunodeficiency virus type-1 integrase)

IT 52350-85-3, Integrase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
((-)-arctigenin as a lead structure for inhibitors of human immunodeficiency virus type-1 integrase)

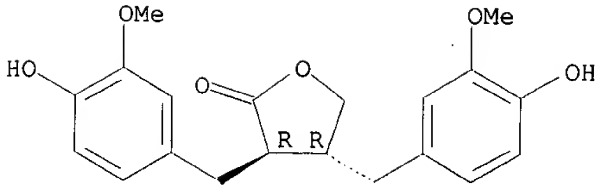
IT 99-24-1, Methyl 3,4,5-trihydroxybenzoate 100-39-0, Benzyl bromide 100-46-9, Benzylamine, reactions 497-23-4, 2(5H)-Furanone 930-30-3, 2-Cyclopentenone 1700-30-7, 3-(Benzyloxy)benzyl alcohol 1700-31-8, 3-(Benzyloxy)benzyl bromide 50766-67-1 56579-86-3
RL: RCT (Reactant); RACT (Reactant or reagent)
((-)-arctigenin as a lead structure for inhibitors of human immunodeficiency virus type-1 integrase)

IT 5544-60-5P 72724-00-6P 171260-21-2P 171260-22-3P 171260-23-4P 171260-24-5P 171260-25-6P 171260-26-7P 171260-27-8P 171260-28-9P 171260-35-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
((-)-arctigenin as a lead structure for inhibitors of human immunodeficiency virus type-1 integrase)

IT **580-72-3P, (-)-Matairesinol**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); **USES (Uses)**
((-)-arctigenin as a lead structure for inhibitors of human immunodeficiency virus type-1 integrase)

RN 580-72-3 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)- (9CI) (CA INDEX NAME)

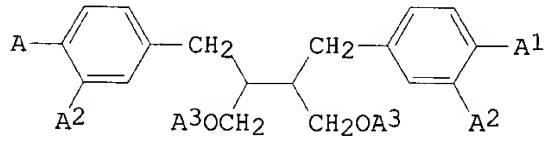
Absolute stereochemistry. Rotation (-).



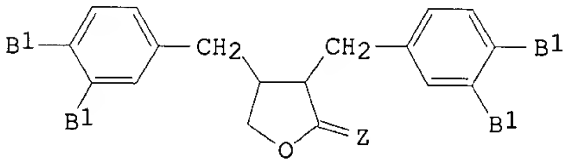
L128 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN 1991:23554 HCAPLUS
DN 114:23554
TI Preparation of dibenzylbutanediol and dibenzyltetrahydrofuran derivatives as immunosuppressants
IN Oka, Kitaro; Hirano, Toshihiko; Naito, Takashi; Hosaka, Kunio
PA Tsumura and Co., Japan
SO Jpn. Kokai Tokkyo Koho, 21 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61K031-05
ICS A61K031-075; A61K031-22; A61K031-34
ICA C07C033-24; C07C039-15; C07C043-20; C07C069-21; C07D307-10; C07D307-33
CC 25-18 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 27, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 02040323	A2	19900209	JP 1988-186853	19880728
PRAI	JP 1988-186853		19880728		

OS MARPAT 114:23554
GI



I



II

AB The title compds. (I, II; A, A1, A2 = H, OH, MeO; A3 = H, Me, Ac; B1 = H, MeO; Z = O, 2H) were prepd. and formulated as immunosuppressants. A soln. of hydrocinnamic acid in THF was added to BuLi-hexane at -72.degree. with stirring under Ar, the soln. warmed to -10.degree., cooled to -62.degree., a soln. of iodine in THF was added to give (.+-.)-2,3-dibenzylsuccinic acid, which was esterified with MeI in DMF under Ar to give the di-Me ester (III). Redn. of III gave diol (.+-.)-I (A = A1 = A2 = A3 = H), which inhibited mitogen-stimulated human peripheral lymphocyte proliferation by 56.8%. Also prepd. and tested were 17 addnl. I and II. Tablet, granular, and injection formulations were also given.

ST immunosuppressant dibenzylbutanediol dibenzyltetrahydrofuran prepn; benzylbutanediol prepn immunosuppressant; benzyltetrahydrofuran prepn

immunosuppressant

IT **Immunosuppressants**
(dibenzylbutanediol and dibenzyltetrahydrofuran derivs.)

IT 501-52-0, Hydrocinnamic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(coupling reaction of)

IT 2316-26-9, 3,4-Dimethoxycinnamic acid 6099-04-3, m-Methoxycinnamic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrogenation of, in prepn. of immunosuppressants)

IT 2107-70-2P, 3,4-Dimethoxyhydrocinnamic acid 10516-71-9P, 3-Methoxydihydrocinnamic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and coupling reaction of, in prepn. of immunosuppressants)

IT 93609-04-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and dehydration of, in prepn. of immunosuppressants)

IT 93578-36-0P 93578-39-3P 119516-58-4P 126965-29-5P 126965-30-8P 126965-33-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and esterification of, in prepn. of immunosuppressants)

IT 121955-01-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and etherification of, in prepn. of immunosuppressants)

IT 126965-31-9P 126981-89-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and lactonization of, in prepn. of immunosuppressants)

IT 81436-89-7P 119516-59-5P 121955-10-0P 126965-28-4P 126965-34-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of, in prepn. of immunosuppressants)

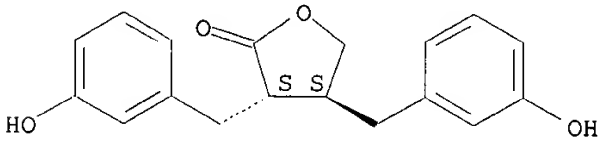
IT 77756-22-0P 77756-23-1P 78473-70-8P **78473-71-9P**
93451-90-2P 119516-60-8P 121851-41-0P 121955-04-2P 121955-05-3P
121955-06-4P 121955-07-5P 121955-09-7P 121986-75-2P 122045-61-8P
122045-63-0P 123808-59-3P 123877-50-9P 131049-50-8P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); **USES (Uses)**
(prepn. of, as immunosuppressant)

IT **78473-71-9P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); **USES (Uses)**
(prepn. of, as immunosuppressant)

RN 78473-71-9 HCAPLUS

CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

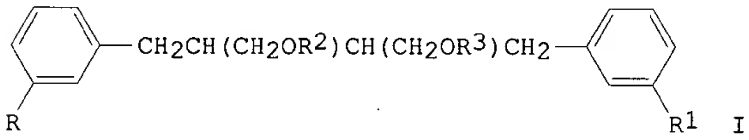
Relative stereochemistry.



L128 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN **1982:162321** HCAPLUS
DN **96:162321**
TI 2,3-Bis(hydroxybenzyl) derivatives
IN Groen, Marinus Bernard
PA AKZO N. V. , Neth.
SO Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DT Patent
LA English
IC C07C039-16; C07C069-017; C07D321-06; A61K031-065; A61K031-215; A61K031-335
CC 25-10 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 43150	A1	19820106	EP 1981-200622	19810605
	R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	ZA 8103951	A	19820630	ZA 1981-3951	19810611
	US 4343796	A	19820810	US 1981-272727	19810611
	DK 8102677	A	19811225	DK 1981-2677	19810618
	AU 8172032	A1	19820107	AU 1981-72032	19810622
	FI 8101967	A	19811225	FI 1981-1967	19810623
	JP 57032239	A2	19820220	JP 1981-97336	19810623
	ES 503338	A1	19821101	ES 1981-503338	19810623
PRAI	GB 1980-20688		19800624		

GI

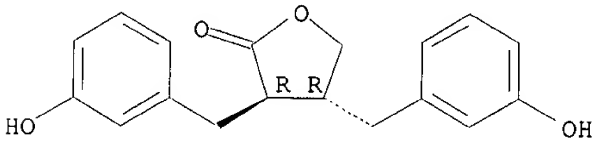


I

AB 1,4-Butanediylbis(phenols) and derivs. I [R and R1 (same or different) are OH, etherified OH, esterified OH; R2 and R3 (same or different) are H, acyl, or R2R3 = alkylidene], useful as antiinflammatory agents (no data), were prepd. (.+-.)-trans-3,4-Bis(3-hydroxybenzyl)-4,5-dihydro-2(3H)-furanone was treated with LiAlH4 in THF to give (.+-.)-I (R = R1 = OH, R2 = R3 = H).
ST phenol butanediylbis prepn antiinflammatory; butanediylbisphenol prepn antiinflammatory
IT **Inflammation inhibitors and Antiarthritics**
(butanediylbis(phenol) derivs.)
IT 123-25-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation reaction of, with methoxybenzaldehyde)
IT 591-31-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation reaction of, with succinate ester)
IT 67-64-1P, preparation
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(ketalization of, by dibenzylbutanediol deriv.)
IT 81436-88-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrogenation of)
IT 81436-89-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

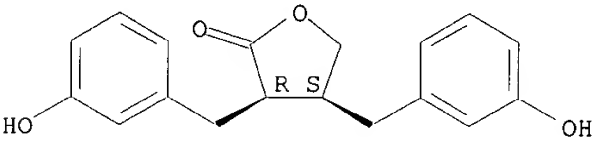
(prepn. and hydrolysis of, and hydride redn. of product from)
IT 77756-22-0P 77756-23-1P 81436-90-0P 81436-91-1P 81436-92-2P
81495-77-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT **76721-88-5 77756-20-8 77756-21-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reductive ring cleavage of)
IT 98-88-4 108-24-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(O-acylation of butanediylbis(phenol) deriv. by)
IT **76721-88-5 77756-20-8 77756-21-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reductive ring cleavage of)
RN 76721-88-5 HCAPLUS
RN 77756-20-8 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 77756-21-9 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, cis- (9CI) (CA
INDEX NAME)

Relative stereochemistry.



=> fil medline
FILE 'MEDLINE' ENTERED AT 16:31:35 ON 06 MAY 2003

FILE LAST UPDATED: 3 MAY 2003 (20030503/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html
for a description on changes.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d all tot

L168 ANSWER 1 OF 11 MEDLINE
AN 2002689618 MEDLINE
DN 22338109 PubMed ID: 12450882
TI Beneficial role of dietary phytoestrogens in obesity and diabetes.

AU Bhathena Sam J; Velasquez Manuel T
CS Phytonutrients Laboratory, Beltsville Human Nutrition Research Center, Agricultural Research Service, US Department of Agriculture, Beltsville, MD 20705, USA.. bhathens@ba.ars.usda.gov
SO AMERICAN JOURNAL OF CLINICAL NUTRITION, (2002 Dec) 76 (6) 1191-201. Ref: 115
Journal code: 0376027. ISSN: 0002-9165.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200212
ED Entered STN: 20021214
Last Updated on STN: 20021221
Entered Medline: 20021220
AB Evidence is emerging that dietary phytoestrogens play a beneficial role in obesity and diabetes. Nutritional intervention studies performed in animals and humans suggest that the ingestion of soy protein associated with isoflavones and flaxseed rich in lignans improves glucose control and insulin resistance. In animal models of obesity and diabetes, soy protein has been shown to reduce serum insulin and insulin resistance. In studies of human subjects with or without diabetes, soy protein also appears to moderate hyperglycemia and reduce body weight, hyperlipidemia, and hyperinsulinemia, supporting its beneficial effects on obesity and diabetes. However, most of these clinical trials were relatively short and involved a small number of patients. Furthermore, it is not clear whether the beneficial effects of soy protein and flaxseed are due to isoflavones (daidzein and genistein), lignans (**matairesinol** and secoisolariciresinol), or some other component. Isoflavones and lignans appear to act through various mechanisms that modulate pancreatic insulin secretion or through antioxidative actions. They may also act via estrogen receptor-mediated mechanisms. Some of these actions have been shown in vitro, but the relevance of these studies to in vivo disease is not known. The diversity of cellular actions of isoflavones and lignans supports their possible beneficial effects on various chronic diseases. Further investigations are needed to evaluate the long-term effects of phytoestrogens on obesity and diabetes mellitus and their associated possible complications.
CT Check Tags: Human
Blood Glucose: ME, metabolism
***Diabetes Mellitus: DT, drug therapy**
*Diet
*Estrogens, Non-Steroidal: AD, administration & dosage
Estrogens, Non-Steroidal: PK, pharmacokinetics
Insulin: BL, blood
Insulin Resistance
Isoflavones: AD, administration & dosage
*Obesity: DT, drug therapy
Phytotherapy
Soybean Proteins: AD, administration & dosage
RN 11061-68-0 (Insulin)
CN 0 (Blood Glucose); 0 (Estrogens, Non-Steroidal); 0 (Isoflavones); 0 (Soybean Proteins); 0 (phytoestrogens)

L168 ANSWER 2 OF 11 MEDLINE
AN 2002148147 MEDLINE
DN 21837925 PubMed ID: 11849672
TI Association between low serum **enterolactone** and increased plasma F2-isoprostanes, a measure of lipid peroxidation.
AU Vanharanta Meri; Voutilainen Sari; Nurmi Tarja; Kaikkonen Jari; Roberts L Jackson; Morrow Jason D; Adlercreutz Herman; Salonen Jukka T

CS Research Institute of Public Health, University of Kuopio, PO Box 1627, 70211 Kuopio, Finland.
NC CA77839 (NCI)
DK26657 (NIDDK)
DK48831 (NIDDK)
GM15431 (NIGMS)
GM42056 (NIGMS)
SO ATHEROSCLEROSIS, (2002 Feb) 160 (2) 465-9.
Journal code: 0242543. ISSN: 0021-9150.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200204
ED Entered STN: 20020308
Last Updated on STN: 20020419
Entered Medline: 20020418
AB Evidence suggests that low serum **enterolactone** concentration might be an independent risk factor for acute coronary events. **Enterolactone** is a lignan, which is formed by intestinal bacteria from precursors in plant foods. Due to the biphenolic structure of **enterolactone**, it could act as an antioxidant and through this contribute to cardiovascular health. The aim of this study was to test the hypothesis that a low serum **enterolactone** concentration is associated with increased in vivo lipid peroxidation, assessed by plasma F2-isoprostane concentrations. We investigated this association in a subset of participants in 'The Antioxidant Supplementation in Atherosclerosis Prevention' (ASAP) study. Out of 256 male participants a subsample of 100 consecutive men from baseline was selected for F2-isoprostane assays. The mean serum **enterolactone** concentration was 16.6 nmol/l and that of F2-isoprostanes 29.6 ng/l. The correlation coefficient for association between serum **enterolactone** and F2-isoprostane concentrations was -0.30 ($P<0.003$). Plasma F2-isoprostane levels decreased linearly across quintiles of serum **enterolactone** concentration ($P=0.008$ for a linear trend). In a multivariate model, **enterolactone** persisted as a significant predictor after adjustment for vitamins and other variables, with the strongest associations with F2-isoprostanes. Our present data suggest that low serum **enterolactone** concentration is associated with enhanced in vivo lipid peroxidation in men.
CT Check Tags: Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*4-Butyrolactone: AA, analogs & derivatives
*4-Butyrolactone: BL, blood
Coronary Disease: BL, blood
Estrogens: BL, blood
*F2-Isoprostanes: BL, blood
Homocysteine: BL, blood
*Lignans: BL, blood
*Lipid Peroxidation
Middle Age
Multivariate Analysis
Risk Factors
RN 454-28-4 (Homocysteine); **76543-15-2 (2,3-bis(3'-hydroxybenzyl)butyrolactone)**; 96-48-0 (4-Butyrolactone)
CN 0 (Estrogens); 0 (F2-Isoprostanes); 0 (Lignans)

L168 ANSWER 3 OF 11 MEDLINE
AN 2001451032 MEDLINE
DN 21367898 PubMed ID: 11473435
TI Anti-AIDS agents. 46. Anti-HIV activity of harman, an anti-HIV principle from Symplocos setchuensis, and its derivatives.
AU Ishida J; Wang H K; Oyama M; Cosentino M L; Hu C Q; Lee K H

CS Natural Products Laboratory, School of Pharmacy, University of North Carolina, Chapel Hill, North Carolina 27599-7360, USA.
NC AI 33066 (NIAID)
SO JOURNAL OF NATURAL PRODUCTS, (2001 Jul) 64 (7) 958-60.
Journal code: 7906882. ISSN: 0163-3864.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200110
ED Entered STN: 20010813
Last Updated on STN: 20011015
Entered Medline: 20011011
AB **Matairesinol** (1) and harman (5), identified from Symplocos setchuensis, were found to inhibit HIV replication in H9 lymphocyte cells. Anti-HIV evaluation of 28 derivatives of 5 revealed that compound 19 showed potent activity with EC(50) and therapeutic index values of 0.037 microM and 210, respectively.
CT Check Tags: Comparative Study; Human; Support, U.S. Gov't, P.H.S.
Anti-HIV Agents: CH, chemistry
*Anti-HIV Agents: IP, isolation & purification
Anti-HIV Agents: PD, pharmacology
Chromatography, High Pressure Liquid
Drugs, Chinese Herbal: CH, chemistry
*Drugs, Chinese Herbal: IP, isolation & purification
Drugs, Chinese Herbal: PD, pharmacology
Furans: CH, chemistry
*Furans: IP, isolation & purification
Furans: PD, pharmacology
Harmine: AA, analogs & derivatives
Harmine: CH, chemistry
*Harmine: IP, isolation & purification
Harmine: PD, pharmacology
Lignans: CH, chemistry
*Lignans: IP, isolation & purification
Lignans: PD, pharmacology
Lymphocytes: DE, drug effects
Lymphocytes: ME, metabolism
Molecular Structure
*Plants, Medicinal: CH, chemistry
Structure-Activity Relationship
RN 442-51-3 (Harmine); 486-84-0 (harman); **580-72-3 (matairesinol)**
CN 0 (Anti-HIV Agents); 0 (Drugs, Chinese Herbal); 0 (Furans); 0 (Lignans); 0 (N-butylharman)

L168 ANSWER 4 OF 11 MEDLINE
AN 2001255072 MEDLINE
DN 21189071 PubMed ID: 11292319
TI In vitro inhibitory effects of Daphne oleoides ssp. oleoides on inflammatory cytokines and activity-guided isolation of active constituents.
AU Yesilada E; Taninaka H; Takaishi Y; Honda G; Sezik E; Momota H; Ohmoto Y; Taki T
CS Faculty of Pharmacy, Gazi University, Etiler, 06330, Ankara, Turkey.. yesilada@pharmacy.gazi.edu.tr
SO CYTOKINE, (2001 Mar 21) 13 (6) 359-64.
Journal code: 9005353. ISSN: 1043-4666.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200107
ED Entered STN: 20010723

Last Updated on STN: 20010723
Entered Medline: 20010719

AB Aerial parts of Daphne oleoides Schreber ssp. oleoides (Thymelaeaceae) are used to treat rheumatoid arthritis and lumbago in Turkish folk medicine. In order to evaluate folkloric utilization, in vitro inhibitory effects of the ethyl acetate extract and fractions obtained from this extract on interleukin 1 (IL-1alpha, IL-1beta) and tumour necrosis factor (TNF-alpha) biosynthesis were studied. Through chemical isolation techniques and activity-guided fractionation process, seventeen compounds were isolated and their structures were elucidated (numbered 1-17). Diterpenoids genkwadaphnin (3) and 1,2-dehydrodaphnetoxin (6) and a coumarin derivative daphnetin (9) showed potent inhibitory activity and were found to be the main active ingredients. Furthermore, gnidilatin (4), gnidilatin-20 palmitate (5), genkwadaphnin-20-palmitate (7) and gnidicin-20-palmitate (8), having diterpenoid structure, and eudesmine (12), wikstromol (13) and **matairesinol** (14), having lignan structure, were determined to possess moderate inhibitory activity and may have a contributory role in the effect of the remedy.

CT Check Tags: Human; Support, Non-U.S. Gov't
Acetates: PD, pharmacology
Antineoplastic Agents, Phytogenic: PD, pharmacology
*Cytokines: ME, metabolism
Diterpenes: PD, pharmacology
Dose-Response Relationship, Drug
Enzyme-Linked Immunosorbent Assay
Free Radical Scavengers: PD, pharmacology
Furans: PD, pharmacology
Interleukin-1: BI, biosynthesis
Interleukin-1: BL, blood
Lignans: PD, pharmacology
Models, Chemical
*Plant Extracts: PD, pharmacology
Plants, Medicinal: CH, chemistry
Tumor Necrosis Factor: BI, biosynthesis
Umbelliferones: PD, pharmacology

RN 141-78-6 (ethyl acetate); 34444-37-6 (nortrachelogenin); 486-35-1 (daphnetin); 526-06-7 (eudesmin); 55073-32-0 (genkwadaphnin); **580-72-3 (matairesinol)**; 60195-70-2 (gnidilatidin)

CN 0 (Acetates); 0 (Antineoplastic Agents, Phytogenic); 0 (Cytokines); 0 (Diterpenes); 0 (Free Radical Scavengers); 0 (Furans); 0 (Interleukin-1); 0 (Lignans); 0 (Plant Extracts); 0 (Tumor Necrosis Factor); 0 (Umbelliferones)

L168 ANSWER 5 OF 11 MEDLINE
AN 2001092417 MEDLINE
DN 21028282 PubMed ID: 11156742
TI Antioxidants in vegan diet and rheumatic disorders.
AU Hanninen; Kaartinen K; Rauma A L; Nenonen M; Torronen R; Hakkinen A S; Adlercreutz H; Laakso J
CS Department of Physiology, University of Kuopio, Finland.. osmo.hanninen@uku.fi
SO TOXICOLOGY, (2000 Nov 30) 155 (1-3) 45-53.
Journal code: 0361055. ISSN: 0300-483X.
CY Ireland
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 200101
ED Entered STN: 20010322
Last Updated on STN: 20010322

Entered Medline: 20010125

AB Plants are rich natural sources of antioxidants in addition to other nutrients. Interventions and cross sectional studies on subjects consuming uncooked vegan diet called living food (LF) have been carried out. We have clarified the efficacy of LF in rheumatoid diseases as an example of a health problem where inflammation is one of the main concerns. LF is an uncooked vegan diet and consists of berries, fruits, vegetables and roots, nuts, germinated seeds and sprouts, i.e. rich sources of carotenoids, vitamins C and E. The subjects eating LF showed highly increased levels of beta and alfa carotenes, lycopen and lutein in their sera. Also the increases of vitamin C and vitamin E (adjusted to cholesterol) were statistically significant. As the berry intake was 3-fold compared to controls the intake of polyphenolic compounds like quercetin, myricetin and kaempherol was much higher than in the omnivorous controls. The LF diet is rich in fibre, substrate of lignan production, and the urinary excretion of polyphenols like enterodiol and **enterolactone** as well as secoisolaricirecinol were much increased in subjects eating LF. The shift of fibromyalgic subjects to LF resulted in a decrease of their joint stiffness and pain as well as an improvement of their self-experienced health. The rheumatoid arthritis patients eating the LF diet also reported similar positive responses and the objective measures supported this finding. The improvement of rheumatoid arthritis was significantly correlated with the day-to-day fluctuation of subjective symptoms. In conclusion the rheumatoid patients subjectively benefited from the vegan diet rich in antioxidants, lactobacilli and fibre, and this was also seen in objective measures.

CT Check Tags: Female; Human
Antioxidants: AN, analysis
*Antioxidants: ME, metabolism
***Arthritis, Rheumatoid: DH, diet therapy**
Arthritis, Rheumatoid: PP, physiopathology
Carotenoids: BL, blood
Chromatography, High Pressure Liquid
*Diet, Vegetarian
Dietary Fiber
Eating
*Fibromyalgia: DH, diet therapy
Fibromyalgia: PP, physiopathology
Flavones: AN, analysis
Fruit: CH, chemistry
Lactobacillus
Lignans: AN, analysis
Middle Age
Severity of Illness Index
Treatment Outcome
Vegetables: CH, chemistry

RN 36-88-4 (Carotenoids)

CN 0 (Antioxidants); 0 (Flavones); 0 (Lignans); 0 (flavonols)

L168 ANSWER 6 OF 11 MEDLINE

AN 2001088332 MEDLINE

DN 20434513 PubMed ID: 10981647

TI A novel treatment for lupus nephritis: lignan precursor derived from flax.

AU Clark W F; Muir A D; Westcott N D; Parbtani A

CS Department of Medicine, London Health Sciences Centre and The University of Western Ontario, Canada.. william.clark@lhsc.on.ca

SO LUPUS, (2000) 9 (6) 429-36.
Journal code: 9204265. ISSN: 0961-2033.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200101

ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010116

AB BACKGROUND: Flaxseed has renoprotective effects in animal and human lupus nephritis. We have recently extracted the lignan precursor (secoisolariresinol diglucoside) (SDG) to determine if this more palatable derivative of flaxseed would exert renoprotection similar to the whole flaxseed in the aggressive MRL/lpr lupus mouse model. METHODS: 131 MRL/lpr mice were randomly assigned to saline gavage, 600, 1,200 and 4,800 microg lignan gavage groups. At 7 weeks, 6 animals underwent platelet aggregating factor (PAF) lethal challenge and 40 were studied with urine collection to determine the levels of secoisolariresinol, enterodiol and **enterolactone** in the gavaged animals. A baseline study of 10 saline gavaged animals took place at 6 weeks. 25 animals in the saline gavage, 600 and 1200 microg lignan groups were studied at 14 and 22 weeks for GFR, spleen lymphocyte S-phase and organ weight studies. RESULTS: Metabolic studies indicated that secoisolariresinol is the major metabolite absorbed and the lowest lignan dose provides a lengthening in survival for the PAF lethal challenge. Body weight, fluid and water intake studies demonstrated that the lignan was well tolerated. Changes in proteinuria, GFR and renal size showed a time- and dose-dependent protection for the lignan precursor. Cervical lymph node size and spleen lymphocyte cells in the S-phase demonstrated modest dose-dependent reductions in the lignan gavaged groups. CONCLUSION: SDG was converted in the gut to secoisolariresinol, which was absorbed and well tolerated by the MRL/lpr mice. Renoprotection was evidenced, in a dose-dependent fashion, by a significant delay in the onset of proteinuria with preservation in GFR and renal size. This study suggests that SDG may have a therapeutic role in lupus nephritis.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
4-Butyrolactone: AA, analogs & derivatives
4-Butyrolactone: UR, urine
Blood Coagulation Factors: ME, metabolism
*Flax: TU, therapeutic use
*Lignans: TU, therapeutic use
Lignans: UR, urine
***Lupus Nephritis: DT, drug therapy**
Lupus Nephritis: ME, metabolism
Lupus Nephritis: PP, physiopathology
Mice
*Phytotherapy
*Seeds

RN **76543-15-2 (2,3-bis(3'-hydroxybenzyl)butyrolactone)**; 76543-16-3 (2,3-bis(3'-hydroxybenzyl)butane-1,4-diol); 96-48-0 (4-Butyrolactone)

CN 0 (Blood Coagulation Factors); 0 (Lignans); 0 (platelet aggregating factor)

L168 ANSWER 7 OF 11 MEDLINE
AN 2000452264 MEDLINE
DN 20462186 PubMed ID: 11006924
TI Phyto-oestrogens and cardiovascular disease risk.
AU van der Schouw Y T; de Kleijn M J; Peeters P H; Grobbee D E
CS Julius Center for Patient Oriented Research, University Medical Center, Utrecht, The Netherlands.
SO NUTRITION, METABOLISM, AND CARDIOVASCULAR DISEASES, (2000 Jun) 10 (3) 154-67. Ref: 134
Journal code: 9111474. ISSN: 0939-4753.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals

EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010301
AB AIM: To present the currently available evidence on the cardiovascular benefits and risks associated with phyto-oestrogens. DATA-SYNTHESIS: Medline search from 1966-1999 updated with cross-check of references of papers with keywords such as phyto-oestrogens, isoflavones, lignans, genistein, daidzein, **enterolactone**, enterodiol, cardiovascular disease, cardiovascular disease risk factors. CONCLUSIONS: Phyto-oestrogens are plant chemicals divided into three main classes: isoflavones, coumestans, and lignans that display oestrogen-like activity due to their ability to bind to the oestrogen receptor. They are found in grains, beans, green vegetables, fruits, nuts, and grasses. Isoflavones are primarily found in soybeans and soy foods. For epidemiological studies of the relation between phyto-oestrogen intake and disease parameters, intake is estimated with several measures, such as biomarkers (concentrations in urine or blood) or dietary questionnaires, though the optimal method is not yet clear. Phyto-oestrogens are considered to act as selective oestrogen receptor modulators (SERM), exerting both oestrogen agonist and antagonist action. Supplementation with isolated soy protein containing the isoflavones genistein and daidzein reduces serum total and LDL-cholesterol and triglycerides in animals and in humans. Vascular reactivity might be improved by supplementation with isolated soy protein or isoflavones isolated from red clover. Studies on atherosclerosis in animals indicate a potential for risk reduction. Evidence in humans is still scanty. The little we know of the effects of regular dietary phyto-oestrogen intake comes from studies in which phyto-oestrogens were added to the usual diet. Most supplementation studies have been conducted with soy isoflavones, whereas the importance of lignans has not been determined, though they could be more important sources than isoflavones in Western populations. Research has been focused on risk factors. Studies of clinically manifest endpoints are urgently needed.
CT Check Tags: Animal; Human
Arteriosclerosis: PC, prevention & control
Bone Density: DE, drug effects
*Cardiovascular Diseases: PC, prevention & control
*Diet
Dietary Supplements
Estrogens, Non-Steroidal: AN, analysis
Estrogens, Non-Steroidal: CH, chemistry
Estrogens, Non-Steroidal: PD, pharmacology
*Estrogens, Non-Steroidal: TU, therapeutic use
MEDLINE
Models, Animal
Neoplasms: PC, prevention & control
Risk Factors
Soybean Proteins: TU, therapeutic use
CN 0 (Estrogens, Non-Steroidal); 0 (Soybean Proteins); 0 (phytoestrogens)

L168 ANSWER 8 OF 11 MEDLINE
AN 2000279404 MEDLINE
DN 20279404 PubMed ID: 10821384
TI **Enterolactone** and coronary events.
CM Comment on: Lancet. 1999 Dec 18-25;354(9196):2112-5
AU Bonnet F; Gilbert R
SO LANCET, (2000 May 6) 355 (9215) 1642-3.
Journal code: 2985213R. ISSN: 0140-6736.
CY ENGLAND: United Kingdom
DT Commentary
Letter
LA English
FS Abridged Index Medicus Journals; Priority Journals

EM 200006
ED Entered STN: 20000616
Last Updated on STN: 20000811
Entered Medline: 20000607
CT Check Tags: Human
*4-Butyrolactone: AA, analogs & derivatives
4-Butyrolactone: BL, blood
***Coronary Disease: BL, blood**
Diabetes Mellitus: BL, blood
*Estrogens: BL, blood
*Lignans: BL, blood
Risk Assessment
RN **76543-15-2 (2,3-bis(3'-hydroxybenzyl)butyrolactone)**; 96-48-0 (4-Butyrolactone)
CN 0 (Estrogens); 0 (Lignans)

L168 ANSWER 9 OF 11 MEDLINE
AN 2000075907 MEDLINE
DN 20075907 PubMed ID: 10609816
TI Risk of acute coronary events according to serum concentrations of **enterolactone**: a prospective population-based case-control study.
CM Comment in: Lancet. 2000 May 6;355(9215):1642-3
AU Vanharanta M; Voutilainen S; Lakka T A; van der Lee M; Adlercreutz H; Salonen J T
CS Research Institute of Public Health, University of Kuopio, Finland.
NC HL 44199 (NHLBI)
SO LANCET, (1999 Dec 18-25) 354 (9196) 2112-5.
Journal code: 2985213R. ISSN: 0140-6736.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200001
ED Entered STN: 20000124
Last Updated on STN: 20000811
Entered Medline: 20000111
AB BACKGROUND: The lignan **enterolactone**, produced by the intestinal microflora from dietary precursors, has been implicated in protection against cancer. We investigated the association of serum **enterolactone** concentration with the risk of acute coronary events in a prospective nested case-control study in middle-aged men from eastern Finland. METHODS: **Enterolactone** was measured by time-resolved fluoroimmunoassay in serum from 167 men who had an average 7.7 years of follow-up to an acute coronary event and from 167 control men. Both cases and controls were from a cohort of 2005 men who had no clinical coronary heart disease (CHD) at baseline. The controls were matched for age, examination year, and residence. Acute coronary events were registered prospectively. FINDINGS: The mean baseline serum **enterolactone** concentration was lower among the cases than the controls (18.2 [SD 21.1] vs 23.5 [18.2] nmol/L, p=0.001). The men in the highest quarter of the **enterolactone** distribution (>30.1 nmol/L) had a 58.8% (95% CI 24.1-77.6, p=0.005) lower risk of acute coronary events than men in the lowest quarter. After adjustment for the nine most strongly predictive risk factors, men in the highest **enterolactone** quarter had a 65.3% (11.9-86.3, p=0.03) lower risk than men in the lowest quarter. INTERPRETATION: Healthy men with high serum concentrations of **enterolactone** had a lower risk of acute coronary events than men with lower concentrations. These findings support the hypothesis that plant-dominated fibre-rich food lowers the risk of CHD.
CT Check Tags: Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*4-Butyrolactone: AA, analogs & derivatives
4-Butyrolactone: BL, blood

Analysis of Variance
Blood Pressure
Case-Control Studies
Cholesterol: BL, blood
***Coronary Disease: BL, blood**
Coronary Disease: ET, etiology
Diet
Finland
Fluoroimmunoassay
Life Style
*Lignans: BL, blood
Middle Age
Prospective Studies
Risk Factors
Smoking: AE, adverse effects
RN 57-88-5 (Cholesterol); **76543-15-2 (2,3-bis(3'-hydroxybenzyl)butyrolactone)**; 96-48-0 (4-Butyrolactone)
CN 0 (Lignans)

L168 ANSWER 10 OF 11 MEDLINE
AN 94366249 MEDLINE
DN 94366249 PubMed ID: 8084211
TI Natural flavonoids and lignans are potent cytostatic agents against human leukemic HL-60 cells.
AU Hirano T; Gotoh M; Oka K
CS Department of Clinical Pharmacology, Tokyo College of Pharmacy, Japan.
SO LIFE SCIENCES, (1994) 55 (13) 1061-9.
Journal code: 0375521. ISSN: 0024-3205.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199410
ED Entered STN: 19941021
Last Updated on STN: 19970203
Entered Medline: 19941011
AB Anti leukemic-cell efficacy of 28 naturally occurring and synthetic flavonoids and 11 naturally occurring lignans on human promyelocytic leukemic cell line HL-60 were examined using MTT assay methods. Differences between anti cell-proliferative activity and cytotoxicity of these compounds were compared with those of 4 clinical anti-cancer agents. Eight of the 28 flavonoids and 4 of the 11 lignans showed considerable suppressive effects on HL-60 cell growth with IC50s ranging from 10-940 ng/ml. Among these compounds, genistein, honokiol, machilin A, **matairesinol**, and arctigenin had the strongest effects with IC50s less than 100 ng/ml, which were almost equivalent to the effects of current anti-cancer agents. The flavonoid genistein and the lignans, however, showed little or no cytotoxicity against HL-60 cells as assessed by dye exclusion tests (LC50s > 2,900 ng/ml), whereas the regular anti-cancer agents had potent cytotoxicity. All of the flavonoids and lignans, except for machilin A and arctigenin, were less effective against growth of human T lymphocytic leukemia cell line MOLT-4. In addition, the flavonoid and the lignans showed little or no inhibiting activity on mitogen-induced blastogenesis of human peripheral-blood lymphocytes. The lignans and genistein were strongly suppressive against incorporations of [3H]thymidine, [3H]uridine, and [3H]leucine into HL-60 cells. These results showed that some of the naturally occurring flavonoids and lignans inhibited HL-60 cell growth with a non-toxic mechanism, possibly via cessation of DNA, RNA, and/or protein synthesis of the leukemic cells.
CT Check Tags: Comparative Study; Human
*Antineoplastic Agents: PD, pharmacology
Cell Division: DE, drug effects
Drug Screening Assays, Antitumor

*Flavones: PD, pharmacology
Leucine: ME, metabolism
*Leukemia, Promyelocytic, Acute: DT, drug therapy
Leukemia, Promyelocytic, Acute: ME, metabolism
Leukemia, Promyelocytic, Acute: PA, pathology
Leukemia, T-Cell: DT, drug therapy
Leukemia, T-Cell: PA, pathology
*Lignans: PD, pharmacology
Lymphocyte Activation: DE, drug effects
Lymphocytes: DE, drug effects
Lymphocytes: IM, immunology
Tetrazolium Salts
Thiazoles
Thymidine: ME, metabolism
Tumor Cells, Cultured: DE, drug effects
Uridine: ME, metabolism
RN 298-93-1 (thiazolyl blue); 50-89-5 (Thymidine); 58-96-8 (Uridine); 61-90-5 (Leucine)
CN 0 (Antineoplastic Agents); 0 (Flavones); 0 (Lignans); 0 (Tetrazolium Salts); 0 (Thiazoles)

L168 ANSWER 11 OF 11 MEDLINE
AN 93085549 MEDLINE
DN 93085549 PubMed ID: 1360514
TI Effect of mammalian lignans on fMLP-induced oxidative bursts in human polymorphonuclear leucocytes.
AU Morikawa M; Fukuchi K; Inoue M; Tsuboi M
CS Department of Pharmacology, Tokyo College of Pharmacy, Japan.
SO JOURNAL OF PHARMACY AND PHARMACOLOGY, (1992 Oct) 44 (10) 859-61. Journal code: 0376363. ISSN: 0022-3573.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199301
ED Entered STN: 19930129
Last Updated on STN: 19950206
Entered Medline: 19930104
AB We examined the effects of mammalian lignans, **enterolactone**, prestegane B and 2,3-dibenzylbutane-1,4-diol (DBB) on superoxide production and luminol-dependent chemiluminescence (LCL) response in human polymorphonuclear leucocytes (PMNs). The three lignans had no direct effect on the responses of human PMNs. DBB and prestegane B enhanced the superoxide production and LCL response induced by formylmethionyl-leucyl-phenylalanine (fMLP), but **enterolactone** inhibited fMLP-induced effects. The effects of DBB were stronger than those of prestegane B and the effects of DBB were inhibited by bromophenacyl bromide, mepacrine, N-(6-aminophenyl)-5-chloro-1-naphthalene, sulphonamide and trifluoroperazine, but not by gossypol, nordihydroguaretic acid, indomethacin, staurosporine, 1-(5-isoquinolinesulphonyl)-2-methylpiperazine dihydrochloride or (R,S)-2-methoxy-3-(octadecyl-carbamoyloxy)-propyl-2-(2-thiazoli o)-ethylphosphate. These results suggest that DBB primes the responses of human PMNs, and the priming effect is caused by the activation of phospholipase A2--and Ca(2+)-calmodulin-pathways, but not by the activation of lipoxygenase, cyclo-oxygenase and protein kinase C or by the release of platelet activating factor.
CT Check Tags: Human; In Vitro
Chemiluminescence
Lignans
*Lignin: PD, pharmacology
*N-Formylmethionine Leucyl-Phenylalanine: PD, pharmacology
***Neutrophils: DE, drug effects**

***Respiratory Burst: DE, drug effects**
Superoxides: AN, analysis
RN 11062-77-4 (Superoxides); 59880-97-6 (N-Formylmethionine Leucyl-Phenylalanine); 9005-53-2 (Lignin)
CN 0 (Lignans)

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L169 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:392225 HCAPLUS
DN 136:380145
TI Prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases by use of **hydroxymatairesinol**, and a pharmaceutical preparation, food additive and food product comprising **hydroxymatairesinol**
IN **Ahotupa, Markku**; Eckerman, Christer; **Kangas, Lauri**; Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni
PA Finland
SO U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. Ser. No. 829,944.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-70
ICS A61K035-78
NCL 514022000
CC 1-12 (Pharmacology)
Section cross-reference(s): 18, 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002061854	A1	20020523	US 2001-972850	20011010
	US 6451849	B1	20020917	US 1999-281094	19990330
	US 2001016590	A1	20010823	US 2001-829944	20010411
PRAI	US 1999-281094	A1	19990330		
	US 2001-829944	A2	20010411		

AB The invention discloses methods for prevention of cancers, certain non-cancerous, hormone-dependent diseases, and/or cardiovascular diseases in a person, based on the administration of **hydroxymatairesinol.**

The invention also discloses a method for increasing the level of **enterolactone** or another metabolite of **hydroxymatairesinol** in a person's serum, thereby causing prevention of a cancer or a certain non-cancerous, hormone-dependent disease in a person, based on administration of **hydroxymatairesinol**. Furthermore, the invention discloses pharmaceutical prepns., food additives, and food products comprising **hydroxymatairesinol**.

ST **hydroxymatairesinol** pharmaceutical food antitumor cardiovascular drug; hormone dependent disease pharmaceutical **hydroxymatairesinol** ; **enterolactone** stimulation therapeutic metabolite **hydroxymatairesinol**

IT Animal cell line
(JEG-3; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Animal cell line
(MCF-7; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Health food
(and designer foods; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Drug delivery systems
(and nutraceuticals; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Food
(and pharmafoods; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Oat
(bran; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Flaxseed
(flour; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Antioxidants
Carrot
Nutrients
Onion (Allium cepa)
Potato (Solanum tuberosum)
Rye
Soybean (Glycine max)
Spruce (Picea abies)
Wheat bran
(**hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Lignans
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Peroxidation
(lipid; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(low-d., oxidn.; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Antitumor agents
(mammary gland; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Mammary gland
(neoplasm, inhibitors; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Bran
(oat; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peroxidn.; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Peroxides, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(radicals; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Wood
(soft; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT Diet
(supplements; **hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT 518-55-8, .alpha.-Conidendrin 9039-48-9, Aromatase 11041-15-9, Conidendric acid 11062-77-4, Superoxide
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT **78473-71-9, Enterolactone** 80226-00-2, Enterodiol
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(**hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT **20268-71-7, Hydroxymatairesinol**
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(**hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

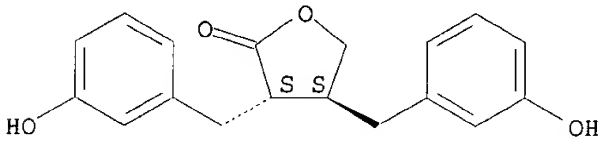
IT 117-39-5, Quercetin 128-37-0, BHT, biological studies 491-54-3, Kaempferide 520-18-3, Kaempferol 25013-16-5, BHA 53188-07-1, Trolox 380448-80-6
RL: PAC (Pharmacological activity); BIOL (Biological study)
(**hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)

IT **20268-71-7D, Hydroxymatairesinol,** (stereo)isomers
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and

pharmaceutical and food products)

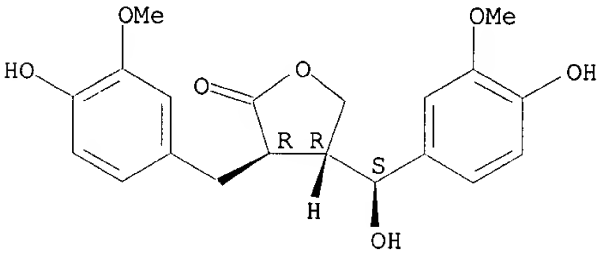
IT **78473-71-9, Enterolactone**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(**hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)
RN 78473-71-9 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



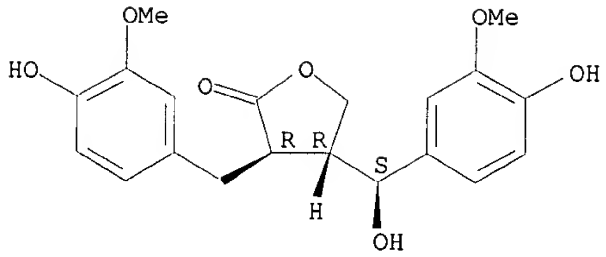
IT **20268-71-7, Hydroxymatairesinol**
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(**hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)
RN 20268-71-7 HCAPLUS
CN 2(3H)-Furanone, dihydro-4-[(S)-hydroxy(4-hydroxy-3-methoxyphenyl)methyl]-3-[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **20268-71-7D, Hydroxymatairesinol,** (stereo)isomers
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**hydroxymatairesinol** for prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases, and pharmaceutical and food products)
RN 20268-71-7 HCAPLUS
CN 2(3H)-Furanone, dihydro-4-[(S)-hydroxy(4-hydroxy-3-methoxyphenyl)methyl]-3-[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L169 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:573545 HCAPLUS
DN 135:132430
TI Decreasing the intracellular level of .beta.-catenin by administering **hydroxymatairesinol**, and therapeutic and diagnostic methods
IN Mutanen, Marja
PA **Hormos Nutraceutical Oy Ltd., Finland**
SO U.S., 7 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-00
NCL 514461000
CC 1-6 (Pharmacology)
Section cross-reference(s): 9
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6271257	B1	20010807	US 2000-550602	20000417
	WO 2001078720	A1	20011025	WO 2001-FI110	20010208
	WO 2001078720	C1	20021212		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1299097	A1	20030409	EP 2001-905844	20010208
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2000-550602	A	20000417		
	WO 2001-FI110	W	20010208		

AB A method is provided for decreasing the intracellular, esp. nuclear, level of .beta.-catenin in an individual. Also provided is a method for the prevention or treatment of a disease or condition in an individual, wherein the disease or condition is related to a mutant APC gene or to an elevated level of intracellular .beta.-catenin. Specifically provided is a method for the treatment of familial adenomatous polyposis. Furthermore, the invention provides methods for screening a subject to det. if said subject is a carrier of a mutant APC gene, as well as methods for diagnosing an individual's predisposition for a disease or condition in an individual, the disease or condition being related to a mutant APC gene or to an elevated level of intracellular .beta.-catenin.
ST **hydroxymatairesinol** therapeutic beta catenin redn; APC gene disease diagnosis therapy **hydroxymatairesinol**; familial adenomatous polyposis treatment **hydroxymatairesinol**
IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(APC; Decreasing the intracellular level of .beta.-catenin by administering **hydroxymatairesinol**, and therapeutic and diagnostic methods)

IT Antitumor agents
Mutation
Rye
(Decreasing the intracellular level of .beta.-catenin by administering **hydroxymatairesinol**, and therapeutic and diagnostic methods)

IT Intestine, neoplasm
(adenoma; Decreasing the intracellular level of .beta.-catenin by administering **hydroxymatairesinol**, and therapeutic and diagnostic methods)

IT Intestine, neoplasm
(familial polyposis; Decreasing the intracellular level of .beta.-catenin by administering **hydroxymatairesinol**, and therapeutic and diagnostic methods)

IT Catenins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.beta.-; Decreasing the intracellular level of .beta.-catenin by administering **hydroxymatairesinol**, and therapeutic and diagnostic methods)

IT **20268-71-7, Hydroxymatairesinol**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Decreasing the intracellular level of .beta.-catenin by administering **hydroxymatairesinol**, and therapeutic and diagnostic methods)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

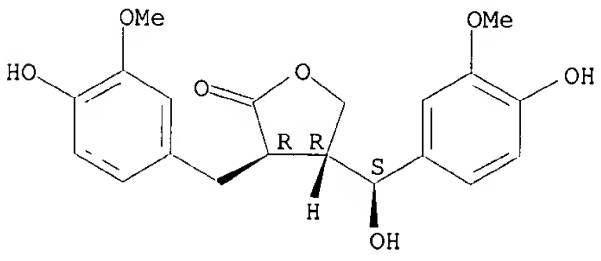
(1) Anon; WO 9213103 1992 HCAPLUS
(2) Barker; US 5998600 1999 HCAPLUS
(3) Bras; European Journal of Cancer Prevention 1999, V8(4), P305 MEDLINE
(4) Herter; Journal of Cancer Research and Clinical Oncology 1999, V125(5) HCAPLUS
(5) Kinzler; US 5709998 1998 HCAPLUS
(6) Mahmoud; Proceeding of the American Association for Cancer Research Annual Meeting 1999, V40, P530
(7) Saarinen; Nutrition and Cancer 2000, V36(2) HCAPLUS

IT **20268-71-7, Hydroxymatairesinol**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Decreasing the intracellular level of .beta.-catenin by administering **hydroxymatairesinol**, and therapeutic and diagnostic methods)

RN 20268-71-7 HCAPLUS

CN 2(3H)-Furanone, dihydro-4-[(S)-hydroxy(4-hydroxy-3-methoxyphenyl)methyl]-3-[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L169 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:725669 HCAPLUS
DN 133:286508
TI **Hydroxymatairesinol** preparations in cancer prevention
IN **Ahotupa, Markku**; Eckerman, Christer; **Kangas, Lauri**; Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni
PA **Hormos Nutraceutical Oy Ltd., Finland**
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K307-32
ICS A61K031-00; A23L001-30
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 17
FAN.CNT 2

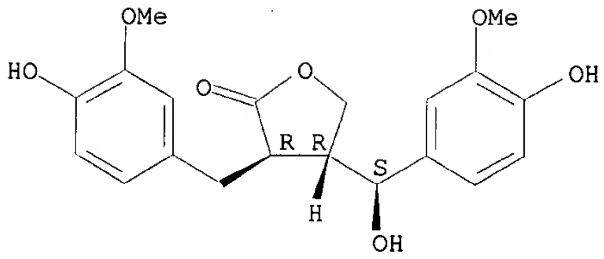
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000059946	A1	20001012	WO 2000-FI181	20000309
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6451849	B1	20020917	US 1999-281094	19990330
	EP 1165537	A1	20020102	EP 2000-909388	20000309
	EP 1165537	B1	20030122		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 2000007187	A	20020219	BR 2000-7187	20000309
	JP 2002541158	T2	20021203	JP 2000-609455	20000309
	EE 200100507	A	20021216	EE 2001-507	20000309
	AT 231500	E	20030215	AT 2000-909388	20000309
	BG 105856	A	20020430	BG 2001-105856	20010830
	NO 2001004639	A	20010925	NO 2001-4639	20010925
PRAI	US 1999-281094	A	19990330		
	WO 2000-FI181	W	20000309		

AB This invention relates to methods for prevention of cancers, certain non-cancer, hormone dependent diseases and/or cardiovascular diseases in a person, based on administering of **hydroxymatairesinol** to said person. The invention also concerns a method for increasing the level of **enterolactone** or another metabolite of **hydroxymatairesinol** in a person's serum thereby causing prevention of a cancer or a certain non-cancer, hormone dependent disease in a person, based on administering of **hydroxymatairesinol** to said person. Furthermore, this invention relates to pharmaceutical prepns., food additives and food products comprising **hydroxymatairesinol**.
ST **hydroxymatairesinol** antitumor hormone disease gynecomastia
IT Lignans
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antioxidant activity of; **hydroxymatairesinol** prepns. in cancer prevention)
IT Prostate gland
(benign hyperplasia; **hydroxymatairesinol** prepns. in cancer prevention)
IT Bakery products

(biscuits; **hydroxymatairesinol** prepns. in cancer prevention)
IT Bakery products
(cakes; **hydroxymatairesinol** prepns. in cancer prevention)
IT Drug delivery systems
(carriers; **hydroxymatairesinol** prepns. in cancer prevention)
IT Intestine, neoplasm
Intestine, neoplasm
(colon, inhibitors; **hydroxymatairesinol** prepns. in cancer prevention)
IT Antitumor agents
(colon; **hydroxymatairesinol** prepns. in cancer prevention)
IT Cardiovascular system
(disease; **hydroxymatairesinol** prepns. in cancer prevention)
IT Hormones, animal, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(diseases dependent on; **hydroxymatairesinol** prepns. in cancer prevention)
IT Urethra
(dyssynergia; **hydroxymatairesinol** prepns. in cancer prevention)
IT Mammary gland
(gynecomastia; **hydroxymatairesinol** prepns. in cancer prevention)
IT Disease, animal
(hormone-dependent; **hydroxymatairesinol** prepns. in cancer prevention)
IT Antioxidants
Antitumor agents
Bread
Butter
Candy
Cardiovascular agents
Confectionery
Food
Food additives
Margarine
(**hydroxymatairesinol** prepns. in cancer prevention)
IT Bladder
(instability; **hydroxymatairesinol** prepns. in cancer prevention)
IT Spruce (Picea abies)
(lignans of; **hydroxymatairesinol** prepns. in cancer prevention)
IT Peroxidation
(lipid; **hydroxymatairesinol** prepns. in cancer prevention)
IT Lipoproteins
RL: ADV (Adverse effect, including toxicity); FMU (Formation, unclassified); BIOL (Biological study); FORM (Formation, nonpreparative)
(low-d., oxidn. products; **hydroxymatairesinol** prepns. in cancer prevention)
IT Urinary tract
(lower, disease; **hydroxymatairesinol** prepns. in cancer prevention)
IT Antitumor agents
(mammary gland; **hydroxymatairesinol** prepns. in cancer prevention)
IT Breakfast cereal
(muesli; **hydroxymatairesinol** prepns. in cancer prevention)
IT Mammary gland
Mammary gland
Prostate gland
Prostate gland

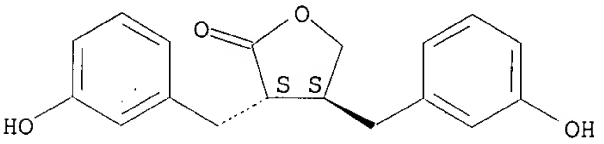
(neoplasm, inhibitors; **hydroxymatairesinol** prepns. in cancer prevention)
IT Bladder
(obstruction; **hydroxymatairesinol** prepns. in cancer prevention)
IT Blood serum
(oxidized LDL of; **hydroxymatairesinol** prepns. in cancer prevention)
IT Pigments, nonbiological
(oxidn. of; **hydroxymatairesinol** prepns. in cancer prevention)
IT Vitamins
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxidn. of; **hydroxymatairesinol** prepns. in cancer prevention)
IT Lipids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(peroxidn.; **hydroxymatairesinol** prepns. in cancer prevention)
IT Antitumor agents
(prostate gland; **hydroxymatairesinol** prepns. in cancer prevention)
IT Milk preparations
(yogurt; **hydroxymatairesinol** prepns. in cancer prevention)
IT **20268-71-7, Hydroxymatairesinol**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**hydroxymatairesinol** prepns. in cancer prevention)
IT **78473-71-9, Enterolactone**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); USES (Uses)
(**hydroxymatairesinol** prepns. in cancer prevention)
IT 9039-48-9, Aromatase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors; **hydroxymatairesinol** prepns. in cancer prevention)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; JP A22000129256 2000 HCAPLUS
(2) Jorma, M; Models in Chemistry 1998, V135(4), P583
(3) Joshua, D; Plant Polyphenols 2: Chemistry, Biology, Pharmacology, Ecology, "Plant ligans and Health:Cancer chemoprevention and biotechnological opportunities" 1999, P675
(4) Kanoldt Arzneimittel Gmbh; WO 9714670 A1 1997 HCAPLUS
IT **20268-71-7, Hydroxymatairesinol**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**hydroxymatairesinol** prepns. in cancer prevention)
RN 20268-71-7 HCAPLUS
CN 2(3H)-Furanone, dihydro-4-[(S)-hydroxy(4-hydroxy-3-methoxyphenyl)methyl]-3-[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **78473-71-9, Enterolactone**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); USES (Uses)
(**hydroxymatairesinol** prepns. in cancer prevention)
RN 78473-71-9 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L169 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:517175 HCAPLUS
DN 133:344260
TI **Hydroxymatairesinol**, a novel **enterolactone** precursor with antitumor properties from a coniferous tree (Picea abies)
AU Saarinen, N. M.; Warri, A.; Makela, S. I.; Eckerman, C.; Reunanen, M.; **Ahotupa, M.**; Salmi, S. M.; Franke, A. A.; **Kangas, L.**; Santti, R.
CS Department of Anatomy and Medical Research Laboratory, University of Turku, Turku, FIN-20520, Finland
SO Nutrition and Cancer (2000), 36(2), 207-214
CODEN: NUCADQ; ISSN: 0163-5581
PB Lawrence Erlbaum Associates, Inc.
DT Journal
LA English
CC 1-6 (Pharmacology)
Section cross-reference(s): 11
AB The plant lignan **hydroxymatairesinol** (HMR) was extd. from Norway spruce (P. abies) and its metab. and biol. actions were studied in animals. HMR, the most abundant single component of spruce lignans, was metabolized to **enterolactone** (ENL) as the major metabolite in rats after oral administration. The amts. of urinary ENL increased with the dose of HMR (3-50 mg/kg), and only minor amts. of unmetabolized HMR isomers and other lignans were found in urine. HMR (15 mg/kg/day for 51 days, orally) decreased the no. of growing tumors and increased the proportion of regressing and stabilized tumors in the rat dimethylbenz[a]anthracene-induced mammary tumor model. HMR (50 mg/kg) had no estrogenic or antiestrogenic activity in the uterine growth test in immature rats. HMR also produced no antiandrogenic responses in the growth of accessory sex glands in adult male rats. Neither ENL nor enterodiol had estrogenic or antiestrogenic activity via the classical .alpha.- or .beta.-type estrogen receptor-mediated pathway in vitro at

<1.0 .mu.M. HMR was an effective antioxidant in vitro.

ST **hydroxymatairesinol enterolactone** antitumor antioxidant Picea abies

IT Androgens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiandrogens; antitumor, antioxidant, and other properties of **hydroxymatairesinol**, a novel **enterolactone** precursor, from Picea abies)

IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiestrogens; antitumor, antioxidant, and other properties of **hydroxymatairesinol**, a novel **enterolactone** precursor, from Picea abies)

IT Antioxidants
Antitumor agents
Spruce (Picea abies)
(antitumor, antioxidant, and other properties of **hydroxymatairesinol**, a novel **enterolactone** precursor, from Picea abies)

IT Lignans
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(antitumor, antioxidant, and other properties of **hydroxymatairesinol**, a novel **enterolactone** precursor, from Picea abies)

IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor, antioxidant, and other properties of **hydroxymatairesinol**, a novel **enterolactone** precursor, from Picea abies)

IT Estrogen receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**hydroxymatairesinol** from Picea abies effect on)

IT 80226-00-2, Enterodiol
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(antitumor, antioxidant, and other properties of **hydroxymatairesinol** and its metabolite enterodiol, from Picea abies)

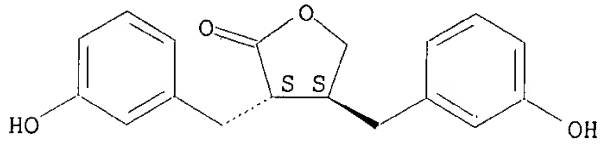
IT **78473-71-9, Enterolactone**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(antitumor, antioxidant, and other properties of **hydroxymatairesinol** and its metabolite **enterolactone**, from Picea abies)

IT **20268-71-7P, Hydroxymatairesinol**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(antitumor, antioxidant, and other properties of **hydroxymatairesinol**, a novel **enterolactone** precursor,

from Picea abies)

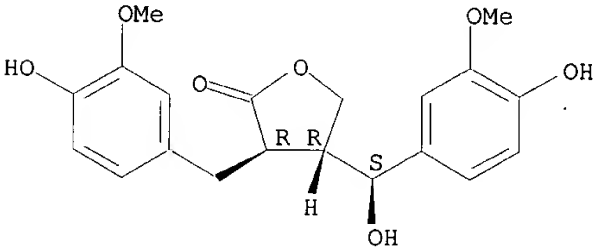
IT **78473-71-9, Enterolactone**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(antitumor, antioxidant, and other properties of **hydroxymatairesinol** and its metabolite **enterolactone**, from Picea abies)
RN 78473-71-9 HCAPLUS
CN 2(3H)-Furanone, dihydro-3,4-bis[(3-hydroxyphenyl)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **20268-71-7P, Hydroxymatairesinol**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(antitumor, antioxidant, and other properties of **hydroxymatairesinol**, a novel **enterolactone** precursor, from Picea abies)
RN 20268-71-7 HCAPLUS
CN 2(3H)-Furanone, dihydro-4-[(S)-hydroxy(4-hydroxy-3-methoxyphenyl)methyl]-3-[(4-hydroxy-3-methoxyphenyl)methyl]-, (3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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E HYDROXYMATAIRESINOL/CN
L2 1 S E3
E ENTEROLACTONE/CN
L3 1 S E3
L4 53 S C20H22O6/MF AND 46.150.18/RID AND OC4/ES AND 3/NR
L5 47 S L4 AND 16.138.1/RID
L6 8 S L5 AND 3 4 BIS 4 HYDROXY 3 METHOXYPHENYL METHYL

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                SEL RN L12
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                SEL RN L16
L19           3 S E10-E14/CRN

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L26         197 S L16
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L29         525 S L22,L25,L28
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                E ERIKSSON J/AU
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                E KOMI J/AU
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                E PERALA M/AU
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                E KORTE H/AU
L37          19 S E3,E4
                E HORMOS/PA,CS
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L39           4 S L29 AND L30-L38
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L40        3039 S E4-E9
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L41       29243 S E6,E5+NT
                E E10+ALL
L42       12864 S E9+NT
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L45           2 S L29 AND L40-L44
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L47       22494 S E21-E23
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                E E17+ALL
L50      167934 S E17+NT
L51      225468 S E16+NT
L52           3 S L29 AND L46-L51
                E MYELOID/CT
                E E12+ALL
L53        2305 S E2
L54           0 S L29 AND L53
L55           1 S L29 AND (TNFALPHA OR ALPHATNF OR ALPHA(A)(TNF OR TUMOR NECROS
L56           1 S L29 AND (TNF OR TUMOR NECROSIS FACTOR)
                E REACTIVE OXYGEN/CT
                E E4+ALL
L57       17391 S E3
L58           0 S L29 AND L57
                E ISCHEMIA/CT
L59           0 S L29 AND E3-E19
                E E3+ALL
L60           0 S L29 AND E5,E4+NT
                E E7+ALL
L61           0 S L29 AND E4
                E E10+ALL
                E E9+ALL
L62           0 S L29 AND E3,E2+NT
L63           0 S L29 AND E1+NT
                E OXIDATIVE BURST/CT
                E E3+ALL
L64           0 S L29 AND E2
L65        5884 S MYELOPEROXIDASE

     FILE 'REGISTRY' ENTERED AT 15:40:40 ON 06 MAY 2003
L66           1 S 9003-99-0
                SEL CHEM

     FILE 'HCAPLUS' ENTERED AT 15:41:06 ON 06 MAY 2003
L67       31161 S L66
L68       74714 S E1-E34
L69           5 S L29 AND L65,L67,L68
                E MYOCARD/CT
                E E12+ALL
                E STROKE/CT
                E E3+ALL
L70           0 S L29 AND E2
                E MYOCARD/CT
                E E12+ALL
L71           0 S L29 AND E2
                E TRANSPLANT/CT
L72           1 S L29 AND E3,E5+NT
                E E3+ALL
                E E3+ALL
L73           1 S L29 AND E7-E12,E6+NT
L74           2 S L29 AND (E34+NT OR E35+NT OR E36+NT OR E37+NT OR E38+NT)
                E ADULT RESPIRATORY DISTRESS/CT
                E E4+ALL
L75           0 S L29 AND E2
                E ENDOTOXIC SHOCK/CT
                E E3+ALL
L76           0 S L29 AND E2
                E HEMMORHAG/CT
                E HEMORHAG/CT
                E E22+ALL
L77           0 S L29 AND E2
```

```
                E RHEUMATOID ARTHRITIS/CT
L78           1 S L29 AND E3-E5
                E E3+ALL
L79           1 S L29 AND E10,E11,E9+NT
                E ALLERGY/CT
L80           0 S L29 AND E3-E16
                E E3+ALL
L81           0 S L29 AND E3,E2+NT
                E E16+ALL
L82           1 S L29 AND (E2 OR E9+NT OR E15+NT)
                E ASTHMA/CT
L83           0 S L29 AND E3-E5
                E E3+ALL
L84           1 S L29 AND (E2 OR E4+NT OR E5+NT OR E6+NT)
                E INFLAMMATION/CT
                E E3+ALL
L85           2 S L29 AND E2+NT
                E E36+ALL
L86           4 S L29 AND E4,E5,E3+NT
                E INFLAMMATORY BOWEL/CT
                E E4+ALL
L87           0 S L29 AND E2
                E SKIN, DISEASE/CT
L88           3 S L29 AND E3+NT
                E HIV/CT
                E E4+ALL
L89           0 S L29 AND E2+NT
                E E2+ALL
L90           0 S L29 AND E7,E8
                E E22+ALL
L91           1 S L29 AND E10
                E E15+ALL
L92           0 S L29 AND E7,E8,E6+NT
                E HUMAN IMMUNODEFICIENCY/CT
L93           2 S L29 AND (E7+NT OR E8+NT OR E9+NT OR E10+NT)
                E PSORIASIS/CT
L94           0 S L29 AND E3-E6
                E E3+ALL
                E PARKINSON/CT
L95           0 S L29 AND E6-E15
                E E6+ALL
L96           0 S L29 AND E4,E3+NT
                E E9+ALL
L97           0 S L29 AND E4+NT
                E ALZHEIMER/CT
L98           0 S L29 AND E9-E15
                E E9+ALL
L99           0 S L29 AND E6,E5+NT
L100         12 S L29 AND (E22+NT OR E23+NT OR E24+NT OR E25+NT OR E26+NT OR E2
                E AUTOIMMUN/CT
                E E8+ALL
L101          1 S L29 AND E3,E2+NT
                E AUTOIMMUNITY/CT
                E E3+ALL
L102          0 S L29 AND E2
                E DIABETES/CT
                E E3+ALL
L103          1 S L29 AND (E1+NT OR E2+NT OR E3+NT)
                E E1+ALL
                E E2+ALL
                E DIABETES/CT
                E E10+ALL
L104          0 S L29 AND E9+NT
```

```
L105          0 S L29 AND E11+NT
                E HYPERCHOLESTEROL/CT
L106          1 S L29 AND E4,E5
                E E4+ALL
                E E4+ALL
L107          4 S L29 AND E5,E6,E4+NT
                E ATHEROSCLEROSIS/CT
L108          0 S L29 AND E3,E4
                E E3+ALL
L109          1 S L29 AND E7-E9,E5+NT
                E E5+ALL
                E E11+ALL
L110          2 S L29 AND E4
                E CATARACT/CT
L111          0 S L29 AND E3-E10
                E E3+ALL
L112          0 S L29 AND E5
                E AMYLOTROPHIC LATERAL/CT
                E ALS/CT
                E E4+ALL
L113          0 S L29 AND E2
L114         37 S L52,L55,L56,L69,L72-L74,L78,L79,L82,L84-L86,L88,L91,L93,L100,
L115         32 S L114 AND L20,L23,L26
L116          5 S L114 NOT L115
                SEL DN AN 1 3
L117          2 S E1-E6 AND L116
                SEL DN AN L115
                SEL DN AN L115 3 4 7 10 17 31
L118          6 S E103-E120 AND L115
L119          8 S L117,L118
L120         26 S L115 NOT L119
L121         74 S (L8 OR L12 OR L16)(L)(THU OR PAC OR PKT OR BUU OR BAC OR USES
L122         16 S L121 AND L114
L123          5 S L119 AND L122
L124          8 S L119,L123
L125         11 S L120 AND L121
L126         19 S L124,L125
L127         15 S L120 NOT L126
L128         19 S L126 AND L20-L65,L67-L127
                SEL  HIT RN

     FILE 'REGISTRY' ENTERED AT 16:19:53 ON 06 MAY 2003
L129          5 S E121-E126
L130         15 S L8,L12,L16,L129

     FILE 'REGISTRY' ENTERED AT 16:21:02 ON 06 MAY 2003

     FILE 'HCAPLUS' ENTERED AT 16:21:15 ON 06 MAY 2003

     FILE 'MEDLINE' ENTERED AT 16:21:32 ON 06 MAY 2003
L131         95 S L130
L132        168 S L21,L24,L27
L133        184 S L131,L132
                E PHAGOCYTE/CT
L134          1 S L133 AND E29+NT
                E E29+ALL
                E LYMPHYOCYTES/CT
                E LYMPHOCYTES/CT
L135          2 S L133 AND E3+NT
                E MYELOID/CT
                E E8+ALL
L136          1 S L133 AND E2+NT
                E TUMOR NECROSIS FACTOR ALPHA/CT
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                E E3+ALL
L137          1 S L133 AND E2+NT
                E OXIDATIVE BURST/CT
                E E3+ALL
L138          1 S L133 AND E2+NT
                E REACTIVE OXYGEN/CT
L139          1 S L133 AND E4+NT
                E ISCHEMIA/CT
L140          3 S L133 AND E3+NT
                E REPERFUSION/CT
L141          0 S L133 AND E3+NT
                E ISCHEMIA/CT
                E MYOCARD/CT
L142          0 S L133 AND E76+NT
                E STROKE/CT
                E E3+ALL
L143          0 S L133 AND E2+NT
                E TRANSPLANTATION/CT
L144          0 S L133 AND E3+NT
                E ADULT RESPIRATORY/CT
                E E4+ALL
L145          0 S L133 AND E2+NT
                E SHOCK/CT
L146          0 S L133 AND E3+NT
                E RHEMATOID ARTHRITIS/CT
                E RHEUMATOID ARTHRITIS/CT
                E E3+ALL
L147          1 S L133 AND E2+NT
                E ALLERGY/CT
L148          0 S L133 AND E5+NT
                E ASTHMA/CT
L149          0 S L133 AND E3+NT
                E INFLAMMATION/CT
L150          0 S L133 AND E3+NT
                E INFLAMMATORY BOWEL/CT
L151          0 S L133 AND E5+NT
L152          2 S L133 AND C17./CT
                E HIV/CT
L153          0 S L133 AND E3+NT
                E AIDS/CT
                E E3+ALL
L154          0 S L133 AND E2+NT
                E PSORIASIS/CT
L155          0 S L133 AND E3+NT
                E PARKSINSON/CT
                E PARKINSON/CT
L156          0 S L133 AND E7+NT
                E ALZHEIMER/CT
                E E8+ALL
L157          0 S L133 AND (E12+NT OR E46+NT OR E47+NT OR E48+NT OR E49+NT OR E
                E AUTOIMMUNE/CT
L158          2 S L133 AND E16+NT
                E DIABETES/CT
                E E3+ALL
L159          2 S L133 AND E2+NT
                E DIABETES/CT
L160          0 S L133 AND E4+NT
                E HYPERCHOLESTEROL/CT
L161          0 S L133 AND E4+NT
                E ATHEROSCLEROSIS/CT
                E E3+ALL
L162          1 S L133 AND E2+NT
                E CATARACT/CT
```

```
L163          0 S L133 AND E3+NT
                E AMYLOTROPH/CT
L164          0 S L133 AND E12+NT
L165         11 S L134-L164
L166         32 S L133 AND A11./CT
L167          3 S L165 AND L166
L168         11 S L165,L167

     FILE 'MEDLINE' ENTERED AT 16:31:35 ON 06 MAY 2003

     FILE 'HCAPLUS' ENTERED AT 16:31:40 ON 06 MAY 2003
L169          4 S L39 NOT L128
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NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
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NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
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NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
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NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
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NEWS 27	Mar 19	APOLLIT offering free connect time in April 2003
NEWS 28	Mar 20	EVENTLINE will be removed from STN
NEWS 29	Mar 24	PATDPAFULL now available on STN
NEWS 30	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 31	Apr 11	Display formats in DGENE enhanced
NEWS 32	Apr 14	MEDLINE Reload
NEWS 33	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 34	Apr 21	Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS 35	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 36	Apr 28	RDISCLOSURE now available on STN
NEWS 37	May 05	Pharmacokinetic information and systematic chemical names added to PHAR

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                                                       ENTRY    SESSION
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=> s hydroxymatairesinol
L1          120 HYDROXYMATAIRESINOL

=> s l1 and matairesinol
L2           53 L1 AND MATAIRESINOL

=> s l2 and enterolactone
L3           16 L2 AND ENTEROLACTONE

=> dup remove l3
PROCESSING COMPLETED FOR L3
L4            5 DUP REMOVE L3 (11 DUPLICATES REMOVED)

=> d l4 1-5 cbib abs

L4   ANSWER 1 OF 5     MEDLINE                              DUPLICATE 1
2003073811  Document Number: 22472537.    PubMed ID: 12583751.   Synthesis of
     (-)-matairesinol, (-)-enterolactone, and
     (-)-enterodiol from the natural lignan hydroxymatairesinol.
```

Eklund Patrik; Lindholm Anna; Mikkola J-P; Smeds Annika; Lehtila Reko; Sjoholm Rainer. (Department of Organic Chemistry, Abo Akademi University, Biskopsgatan 8, 20500-FIN, Abo, Finland.) ORGANIC LETTERS, (2003 Feb 20) 5 (4) 491-3. Journal code: 100890393. ISSN: 1523-7060. Pub. country: United States. Language: English.

AB We describe here a four-step semisynthetic method for the preparation of enantiomerically pure (-)-**enterolactone** starting from the readily available lignan **hydroxymatairesinol** from Norway spruce (Picea abies). **Hydroxymatairesinol** was first hydrogenated to **matairesinol**. **Matairesinol** was esterified to afford the matairesinyl 4,4'-bistriflate, which was deoxygenated by palladium-catalyzed reduction to 3,3'-dimethylenterolactone. Demethylation of 3,3'-dimethylenterolactone and reduction with LiAlH(4) yielded (-)-**enterolactone** and (-)-enterodiol, respectively.

L4 ANSWER 2 OF 5 MEDLINE DUPLICATE 2

2002484700 Document Number: 22231703. PubMed ID: 12270222. Structural determinants of plant lignans for the formation of **enterolactone** in vivo. Saarinen Niina M; Smeds Annika; Makela Sari I; Ammala Jenni; Hakala Kristo; Pihlava Juha-Matti; Ryhanen Eeva-Liisa; Sjoholm Rainer; Santti Risto. (Department of Anatomy, Institute of Biomedicine, University of Turku, FIN-20520, Turku, Finland.) J Chromatogr B Analyt Technol Biomed Life Sci, (2002 Sep 25) 777 (1-2) 311-9. Journal code: 101139554. ISSN: 1570-0232. Pub. country: United States. Language: English.

AB The quantity of mammalian lignans **enterolactone** (ENL) and enterodiol (END) and of plant lignans secoisolariciresinol (SECO) and 7-**hydroxymatairesinol** (HMR) excreted in a 24-h rat urine sample was measured after a single p.o. dose of an equivalent quantity of secoisolariciresinol diglycoside (SDG), secoisolariciresinol (SECO), **matairesinol** (MR), 7-**hydroxymatairesinol** (HMR) and ENL. Plant lignans (SECO and HMR) were partially absorbed as such. The aglycone form of SECO was more efficiently converted into mammalian lignans END and ENL than the glycosylated form, SDG. Of plant lignans, MR produced the highest quantities of ENL: the quantity was over twofold compared with HMR or SDG. The majority of the animals, which had been given SECO, excreted higher quantities of END than ENL into urine, but ENL was the main lignan metabolite after SDG. The highest quantities of ENL in urine were measured after the administration of ENL as such. The (-)SECO isolated from Araucaria angustifolia was converted into (-)ENL only. The administration of (-)SDG, which was shown to produce (+)SECO, resulted in excretion of (+)ENL only and (-)HMR was converted into (-)ENL only. This confirmed that the absolute configurations at C8 and C8' are not changed during the microbial metabolism. Whether the biological effects are enantiomer-specific, remains to be resolved.

L4 ANSWER 3 OF 5 MEDLINE DUPLICATE 3

2001423900 Document Number: 21347776. PubMed ID: 11453749. In vitro metabolism of plant lignans: new precursors of mammalian lignans **enterolactone** and enterodiol. Heinonen S; Nurmi T; Liukkonen K; Poutanen K; Wahala K; Deyama T; Nishibe S; Adlercreutz H. (Folkhalsan Research Center and Department of Clinical Chemistry, P.O. Box 60, FIN-00014 University of Helsinki, Finland.) JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY, (2001 Jul) 49 (7) 3178-86. Journal code: 0374755. ISSN: 0021-8561. Pub. country: United States. Language: English.

AB The metabolism of the plant lignans **matairesinol**, secoisolariciresinol, pinoresinol, syringaresinol, arctigenin, 7-**hydroxymatairesinol**, isolariciresinol, and lariciresinol by human fecal microflora was investigated to study their properties as mammalian lignan precursors. The quantitative analyses of lignan precursors and the mammalian lignans **enterolactone** and enterodiol were performed by HPLC with coulometric electrode array detector. The metabolic products, including mammalian lignans, were characterized as trimethylsilyl

derivatives by gas chromatography-mass spectrometry. **Matairesinol**, secoisolariciresinol, lariciresinol, and pinoresinol were converted to mammalian lignans only. Several metabolites were isolated and tentatively identified as for syringaresinol and arctigenin in addition to the mammalian lignans. Metabolites of 7-**hydroxymatairesinol** were characterized as **enterolactone** and 7-hydroxyenterolactone by comparison with authentic reference compounds. A metabolic scheme describing the conversion of the most abundant new mammalian lignan precursors, pinoresinol and lariciresinol, is presented.

L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS
2002:543197 Document No. 137:216291 Uptake and metabolism of **hydroxymatairesinol** in relation to its anticarcinogenicity in DMBA-induced rat mammary carcinoma model. Saarinen, Niina M.; Huovinen, Riikka; Waerri, Anni; Maekelae, Sari I.; Valentin-Blasini, Liza; Needham, Larry; Eckerman, Christer; Collan, Yrjoe U.; Santti, Risto (Department of Anatomy, Institute of Biomedicine, University of Turku, Turku, FIN-20520, Finland). Nutrition and Cancer, 41(1&2), 82-90 (English) 2001. CODEN: NUCADQ. ISSN: 0163-5581. Publisher: Lawrence Erlbaum Associates, Inc..

AB The chemopreventive effects of **hydroxymatairesinol** (HMR), a lignan extd. from Norway spruce (Picea abies), on the development of mammary carcinoma induced by 7,12-dimethylbenz[a]anthracene (DMBA) was studied in rats. HMR administered via diet in an av. daily dose of 4.7 mg/kg body wt starting before DMBA induction reduced tumor vol. and tumor growth, but no significant redn. in tumor multiplicity (no. of tumors/rat) was obsd. The predominant histol. type in the control group was type B (well-differentiated adenocarcinoma, 78%). The proportion of type B tumors decreased to 35% in the HMR group, while the type A (poorly differentiated) and type C (atrophic) tumor proportions increased. Anticarcinogenic effects of dietary HMR (4.7 mg/kg) were also evident when the administration started after DMBA induction and was seen as growth inhibition of established tumors. Dietary HMR supplementation significantly increased serum and urinary **enterolactone** and HMR concns. but had no significant effect on the uterine wt., suggesting that HMR or its major metabolite **enterolactone** did not have an anti-estrogenic effect. Further studies are warranted to further clarify and verify HMR action and the assocd. mechanisms in mammary tumorigenesis.

L4 ANSWER 5 OF 5 MEDLINE DUPLICATE 4
2001103469 Document Number: 20348508. PubMed ID: 10890032.
Hydroxymatairesinol, a novel **enterolactone** precursor with antitumor properties from coniferous tree (Picea abies). Saarinen N M; Warri A; Makela S I; Eckerman C; Reunanen M; Ahotupa M; Salmi S M; Franke A A; Kangas L; Santti R. (Department of Anatomy, University of Turku, Finland.) NUTRITION AND CANCER, (2000) 36 (2) 207-16. Journal code: 7905040. ISSN: 0163-5581. Pub. country: United States. Language: English.

AB The potential for the extraction of the plant lignan **hydroxymatairesinol** (HMR) in large scale from Norway spruce (Picea abies) has given us the opportunity to study the metabolism and biological actions of HMR in animals. HMR, the most abundant single component of spruce lignans, was metabolized to **enterolactone** (ENL) as the major metabolite in rats after oral administration. The amounts of urinary ENL increased with the dose of HMR (from 3 to 50 mg/kg), and only minor amounts of unmetabolized HMR isomers and other lignans were found in urine. HMR (15 mg/kg body wt po) given for 51 days decreased the number of growing tumors and increased the proportion of regressing and stabilized tumors in the rat dimethylbenz[a]anthracene-induced mammary tumor model. HMR (50 mg/kg body wt) did not exert estrogenic or antiestrogenic activity in the uterine growth test in immature rats. HMR also showed no antiandrogenic responses in the growth of accessory sex glands in adult male rats. Neither ENL nor enterodiol showed estrogenic

or antiestrogenic activity via a classical alpha- or beta-type estrogen receptor-mediated pathway in vitro at < 1.0 microM. HMR was an effective antioxidant in vitro.

=> s l1 and lignan
L5 105 L1 AND LIGNAN

=> s l5 and phagocytes
L6 0 L5 AND PHAGOCYTES

=> s l5 and oxidative burst
L7 0 L5 AND OXIDATIVE BURST

=> s l5 and neutrophils
L8 0 L5 AND NEUTROPHILS

=> s l5 and myeloid
L9 0 L5 AND MYELOID

=> dup remove l5
PROCESSING COMPLETED FOR L5
L10 53 DUP REMOVE L5 (52 DUPLICATES REMOVED)

=> d l10 1-53 cbib abs

L10 ANSWER 1 OF 53 MEDLINE DUPLICATE 1
2003073811 Document Number: 22472537. PubMed ID: 12583751. Synthesis of (-)-matairesinol, (-)-enterolactone, and (-)-enterodiol from the natural **lignan hydroxymatairesinol**. Eklund Patrik; Lindholm Anna; Mikkola J-P; Smeds Annika; Lehtila Reko; Sjoholm Rainer. (Department of Organic Chemistry, Abo Akademi University, Biskopsgatan 8, 20500-FIN, Abo, Finland.) ORGANIC LETTERS, (2003 Feb 20) 5 (4) 491-3. Journal code: 100890393. ISSN: 1523-7060. Pub. country: United States. Language: English.

AB We describe here a four-step semisynthetic method for the preparation of enantiomerically pure (-)-enterolactone starting from the readily available **lignan hydroxymatairesinol** from Norway spruce (Picea abies). **Hydroxymatairesinol** was first hydrogenated to matairesinol. Matairesinol was esterified to afford the matairesinyl 4,4'-bistriflate, which was deoxygenated by palladium-catalyzed reduction to 3,3'-dimethylenterolactone. Demethylation of 3,3'-dimethylenterolactone and reduction with LiAlH(4) yielded (-)-enterolactone and (-)-enterodiol, respectively.

L10 ANSWER 2 OF 53 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 2
2003:215206 The Genuine Article (R) Number: 650RC. **Lignans** and lipophilic extractives in Norway spruce knots and stemwood. Willfor S (Reprint); Hemming J; Reunanen M; Eckerman C; Holmbom B. Abo Akad Univ, Proc Chem Grp, Lab Forest Prod Chem, Porthansgatan 3, SF-20500 Turku, Finland (Reprint); Abo Akad Univ, Proc Chem Grp, Lab Forest Prod Chem, SF-20500 Turku, Finland. HOLZFORSCHUNG (JAN 2003) Vol. 57, No. 1, pp. 27-36. Publisher: WALTER DE GRUYTER & CO. GENTHINER STRASSE 13, D-10785 BERLIN, GERMANY. ISSN: 0018-3830. Pub. country: Finland. Language: English .

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The hydrophilic and lipophilic extractives in the heartwood of knots from 7 Norway spruce trees were analysed by GC, GC-MS and HPSEC. The knots contained extremely large amounts of **lignans**, 6-24 % (w/w), with **hydroxymatairesinol** comprising 65-85 % of the **lignans**. Even the knots of the young trees contained 4-8 % (w/w) of **lignans** . The variation in the amount of **lignans** was large among knots,

both within a single tree and between trees. In addition to the **lignans**, knots also contained 2-6 % (w/w) of a complex mixture of **lignan**-like compounds with 3,4 and even up to 6 phenyl propane units, here called oligolignans. The amounts of **lignans** in the knots were similar in the radial direction from the pith into the outer branch, but decreased dramatically outwards in the branch, almost disappearing after 10-20 cm. The ratio of the 2 epimers of **hydroxymatairesinol** differed between different knots and even within the knot. A new spruce **lignan**, nortrachelogenin, or its enantiomer, wikstromol, was detected in knots from trees in northern Finland as opposed to samples from southern Finland. ne amount of lipophilic extractives was small compared to the amount of hydrophilic extractives in the knots. Five of the dead knots contained more resin acids and free diterpenyl alcohols than ordinary stemwood. In the other knots, the amount of lipophilic extractives was on the same level as stem heartwood. The stem sapwood contained larger amounts of esterified fatty acids than the knots.

L10 ANSWER 3 OF 53 CAPLUS COPYRIGHT 2003 ACS

2002:946245 Document No. 138:12731 A method for isolating phenolic substances or juvabiones from wood comprising knotwood. Holmbom, Bjarne; Eckerman, Christer; Hemming, Jarl; Reunanen, Markku; Sundberg, Kenneth; Willfoer, Stefan (Finland). PCT Int. Appl. WO 2002098830 A1 20021212, 31 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-FI418 20020516. PRIORITY: US 2001-PV295797 20010606; FI 2001-1194 20010606.

AB The present invention relates to a method for isolating of phenolic substances or juvabiones from wood comprising knotwood, said method comprising the steps of extg. the oversized chip fraction obtained by screening chipped wood, or a knot-rich sub-fraction obtained from said oversized chip fraction, or knotwood obtained as a residue in finishing of mech. wood products, with a polar solvent, and recovering the ext.

L10 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2003 ACS

2002:391957 Document No. 136:387621 Method for recovering non-fibrous substances from wood material processing. Sundberg, Kenneth; Holmbom, Bjarne; Eckerman, Christer; Adams, Maria (Raisio Chemicals Ltd., Finland). PCT Int. Appl. WO 2002040767 A1 20020523, 31 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-FI990 20011115. PRIORITY: FI 2000-2519 20001116.

AB Non-fibrous substances, such as wood resins, arom. components, salts and polysaccharides, are extd. from the wood material into a liq. fraction, such as process water or other suitable water-based liq. The recovery of nonfibrous substances from the liq. fraction includes sepn. of arom. compds. from the liq. fraction, while preferably maintaining to pH <7, during the extg. and recovering processes.

L10 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS

2002:392225 Document No. 136:380145 Prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases by use of **hydroxymatairesinol**, and a pharmaceutical preparation, food additive and food product comprising **hydroxymatairesinol**. Ahotupa, Markku; Eckerman, Christer; Kangas, Lauri; Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni (Finland). U.S. Pat. Appl. Publ. US 2002061854 A1 20020523, 15 pp., Cont.-in-part of U.S. Ser. No. 829,944. (English). CODEN: USXXCO. APPLICATION: US 2001-972850 20011010. PRIORITY: US 1999-281094 19990330; US 2001-829944 20010411.

AB The invention discloses methods for prevention of cancers, certain non-cancerous, hormone-dependent diseases, and/or cardiovascular diseases in a person, based on the administration of **hydroxymatairesinol**. The invention also discloses a method for increasing the level of enterolactone or another metabolite of **hydroxymatairesinol** in a person's serum, thereby causing prevention of a cancer or a certain non-cancerous, hormone-dependent disease in a person, based on administration of **hydroxymatairesinol**. Furthermore, the invention discloses pharmaceutical prepns., food additives, and food products comprising **hydroxymatairesinol**.

L10 ANSWER 6 OF 53 MEDLINE DUPLICATE 3

2002619318 Document Number: 22263729. PubMed ID: 12375994. Synthesis of R-(-)-imperanene from the natural **lignan hydroxymatairesinol**. Eklund Patrik C; Riska Annika I; Sjoholm Rainer E. (Department of Organic Chemistry, Process Chemistry Group, Abo Akademi University, Piispankatu 8, FIN-20500 Turku, Finland.. paeklund@abo.fi) . JOURNAL OF ORGANIC CHEMISTRY, (2002 Oct 18) 67 (21) 7544-6. Journal code: 2985193R. ISSN: 0022-3263. Pub. country: United States. Language: English.

AB A convenient and high yielding method for the synthesis of R-(-)-imperanene, starting from the readily available natural **lignan hydroxymatairesinol** from Norway spruce, was developed. **Hydroxymatairesinol** was degraded in strongly basic aqueous conditions to (E)-4-(4-hydroxy-3-methoxyphenyl)-2-(4-hydroxy-3-methoxyphenylmethyl)but-3-enoic acid, which was esterified and then reduced by LiAlH(4) to afford R-(-)-imperanene. The configuration at the crucial stereocenter was preserved in the synthesis, and the obtained product was identified by optical rotation measurements and chiral HPLC analyses as the R-(-)-enantiomer (ee 86-92%).

L10 ANSWER 7 OF 53 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 4

2002:746504 The Genuine Article (R) Number: 590HU. Synthetic transformation of **hydroxymatairesinol** from Norway spruce (Picea abies) to 7-hydroxysecoisolariciresinol, (+)-lariciresinol and (+)-cyclolariciresinol. Eklund P (Reprint); Sillanpaa R; Sjoholm R. Abo Akad Univ, Dept Organ Chem, Piispankatu 8, FIN-20500 Turku, Finland (Reprint); Abo Akad Univ, Dept Organ Chem, FIN-20500 Turku, Finland; Abo Akad Univ, Dept Organ Chem, Proc Chem Grp, FIN-20500 Turku, Finland; Univ Jyvaskyla, Dept Chem, FIN-40351 Jyvaskyla, Finland. JOURNAL OF THE CHEMICAL SOCIETY-PERKIN TRANSACTIONS 1 (21 AUG 2002) No. 16, pp. 1906-1910. Publisher: ROYAL SOC CHEMISTRY. THOMAS GRAHAM HOUSE, SCIENCE PARK, MILTON RD,, CAMBRIDGE CB4 0WF, CAMBS, ENGLAND. ISSN: 1472-7781. Pub. country: Finland. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have developed a method for the transformation of **hydroxymatairesinol** to optically pure (+)-lariciresinol and (+)-cyclolariciresinol via the hitherto unreported **lignan** 7-hydroxysecoisolariciresinol. The two naturally occurring isomers of **hydroxymatairesinol** were reduced with LiAlH4, to a mixture of two epimers or 7-hydroxysecoisolariciresinol, which were further selectively transformed to (+)-lariciresinol and (+)-cyclolariciresinol by an acid catalysed intramolecular cyclisation reaction. The Structure of the major

isomer of 7-hydroxysecoisolariciresinol was confirmed by X-ray crystallography and thereby also the absolute configurations of the two isomers of **hydroxymatairesinol** were unambiguously proven Optical purities were determined by chiral HPLC-MS/MS and optical rotation measurements.

L10 ANSWER 8 OF 53 SCISEARCH COPYRIGHT 2003 THOMSON ISI
2003:33041 The Genuine Article (R) Number: 626TD. Modification of spruce **lignans** with Trametes hirsuta laccase. Buchert J (Reprint); Mustranta A; Tamminen T; Spetz P; Holmbom B. VTT Biotechnol, POB 1500, Espoo, Finland (Reprint); VTT Biotechnol, Espoo, Finland; KCL, Espoo 02151, Finland; Abo Akad Univ, Proc Chem Grp, SF-20500 Turku, Finland. HOLZFORSCHUNG (DEC 2002) Vol. 56, No. 6, pp. 579-584. Publisher: WALTER DE GRUYTER & CO. GENTHINER STRASSE 13, D-10785 BERLIN, GERMANY. ISSN: 0018-3830. Pub. country: Finland. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The effect of Trametes hirsuta laccase on isolated spruce wood **lignans** was evaluated. **Lignans** were isolated from the heartwood of spruce branches and treated with different laccase dosages and treatment times. The effect of the treatment was monitored by gas chromatography, size exclusion chromatography and ionization difference UV spectroscopy. **Lignans** were efficiently oxidized by T hirsuta laccase. About half of the phenolic groups present in **lignans** remained intact during the treatment. The oxidation of phenolic groups in **lignans** produced oligomeric structures containing approximately 4-5 **lignan** units (i.e., 8-10 phenyl propane units). Precipitation of the formed oligomeric structures probably prevented further polymerization.

L10 ANSWER 9 OF 53 MEDLINE DUPLICATE 5
2002484700 Document Number: 22231703. PubMed ID: 12270222. Structural determinants of plant **lignans** for the formation of enterolactone in vivo. Saarinen Niina M; Smeds Annika; Makela Sari I; Ammala Jenni; Hakala Kristo; Pihlava Juha-Matti; Ryhanen Eeva-Liisa; Sjoholm Rainer; Santti Risto. (Department of Anatomy, Institute of Biomedicine, University of Turku, FIN-20520, Turku, Finland.) J Chromatogr B Analyt Technol Biomed Life Sci, (2002 Sep 25) 777 (1-2) 311-9. Journal code: 101139554. ISSN: 1570-0232. Pub. country: United States. Language: English.
AB The quantity of mammalian **lignans** enterolactone (ENL) and enterodiol (END) and of plant **lignans** secoisolariciresinol (SECO) and 7-**hydroxymatairesinol** (HMR) excreted in a 24-h rat urine sample was measured after a single p.o. dose of an equivalent quantity of secoisolariciresinol diglycoside (SDG), secoisolariciresinol (SECO), matairesinol (MR), 7-**hydroxymatairesinol** (HMR) and ENL. Plant **lignans** (SECO and HMR) were partially absorbed as such. The aglycone form of SECO was more efficiently converted into mammalian **lignans** END and ENL than the glycosylated form, SDG. Of plant **lignans**, MR produced the highest quantities of ENL: the quantity was over twofold compared with HMR or SDG. The majority of the animals, which had been given SECO, excreted higher quantities of END than ENL into urine, but ENL was the main **lignan** metabolite after SDG. The highest quantities of ENL in urine were measured after the administration of ENL as such. The (-)SECO isolated from Araucaria angustifolia was converted into (-)ENL only. The administration of (-)SDG, which was shown to produce (+)SECO, resulted in excretion of (+)ENL only and (-)HMR was converted into (-)ENL only. This confirmed that the absolute configurations at C8 and C8' are not changed during the microbial metabolism. Whether the biological effects are enantiomer-specific, remains to be resolved.

L10 ANSWER 10 OF 53 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 6
2002275982 EMBASE Interactions between **lignans** and probiotics.

Lahtinen S.; Saarinen N.M.; Ammala J.; Makela S.I.; Salminen S.; Ouwehand A.C.. A.C. Ouwehand, Functional Foods Forum, University of Turku, FIN-20014 Turku, Finland. arthur.ouwehand@utu.fi. Microbial Ecology in Health and Disease 14/2 (106-109) 2002.
Refs: 13.
ISSN: 0891-060X. CODEN: MEHDE6. Pub. Country: Norway. Language: English. Summary Language: English.

AB A diet rich in plant **lignans** has been suggested to have anti-cancer properties. Also selected probiotics are suggested to have anti-tumour activity. In the current study the interactions between the plant **lignan** 7-**hydroxymatairesinol** (HMR) and five selected probiotic microorganisms was investigated. The results showed that presence of HMR affected the growth of Lactobacillus johnsonii La1. Compared with the control, the growth was slower during the exponential growth phase when L. johnsonii La1 was cultured in the presence of HMR. Differences in the growth of the other four microorganisms were not statistically significant. The in vitro adhesion of L. casei Shirota to intestinal mucus was found to be more than doubled after growth in the presence of HMR. No conversion of HMR was observed by any of the five tested strains. The data obtained from these experiments suggest that plant **lignans** have some influence on probiotics. However, the mechanisms and the in vivo relevance of these interactions have yet to be resolved. The tested probiotics do not participate in the conversion of plant **lignans** to their biologically active form.

L10 ANSWER 11 OF 53 MEDLINE DUPLICATE 7

2003059990 Document Number: 22457755. PubMed ID: 12570335. Antioxidant and antitumor effects of **hydroxymatairesinol** (HM-3000, HMR), a **lignan** isolated from the knots of spruce. Kangas Lauri; Saarinen Niina; Mutanen Marja; Ahotupa Markku; Hirsinummi Riikka; Unkila Mikko; Perala Merja; Soininen Pasi; Laatikainen Reino; Korte Helena; Santti Risto. (Hormos Nutraceutical Ltd, Turku, Finland.) EUROPEAN JOURNAL OF CANCER PREVENTION, (2002 Aug) 11 Suppl 2 S48-57. Journal code: 9300837. ISSN: 0959-8278. Pub. country: England: United Kingdom. Language: English.

AB The antioxidant properties of **hydroxymatairesinol** (HM-3000) were studied in vitro in lipid peroxidation, superoxide and peroxyl radical scavenging, and LDL-oxidation models in comparison with the known synthetic antioxidants Trolox (a water-soluble vitamin E derivative), butylated hydroxyanisol (BHA) and butylated hydroxytoluene (BHT). On a molar basis HM-3000 was a more effective antioxidant than Trolox in all assays and more effective than BHT or BHA in lipid peroxidation and superoxide scavenging test. The in vivo antioxidative effect (evaluated as the weight gain of C57BL/6J mice fed an alpha-tocopherol-deficient diet) of HM-3000 (500 mg/kg per day) was comparable to that of DL-alpha-tocopherol (766 mg/kg per day). The antitumor activity of HM-3000 was studied in dimethylbenz[a]anthracene (DMBA)-induced rat mammary cancer. HM-3000 had a statistically significant inhibitory effect on tumor growth. Prevention of tumor formation was also evaluated in the Apc(Min) mice model, which develops intestinal polyps spontaneously. HM-3000 was given in diet at 30 mg/kg per day and decreased the formation of polyps and prevented beta-catenin accumulation into the nucleus, the pathophysiological hallmark of polyp formation in this mouse model. In short-term toxicity studies (up to 28 days) HM-3000 was essentially non-toxic when given p.o. to rats and dogs (daily doses up to 2000 and 665 mg/kg, respectively); HM-3000 was shown to be well absorbed (> 50% of the dose) and rapidly eliminated. In human studies HM-3000 has been given in single doses up to 1350 mg to healthy male volunteers without treatment-related adverse events. Rapid absorption from the gastrointestinal tract and partial metabolism to enterolactone in humans was demonstrated. In summary, HM-3000 is a safe, novel enterolactone precursor **lignan** with antioxidant and antitumor properties.

L10 ANSWER 12 OF 53 MEDLINE DUPLICATE 8
2001423900 Document Number: 21347776. PubMed ID: 11453749. In vitro metabolism of plant **lignans**: new precursors of mammalian **lignans** enterolactone and enterodiol. Heinonen S; Nurmi T; Liukkonen K; Poutanen K; Wahala K; Deyama T; Nishibe S; Adlercreutz H. (Folkhalsan Research Center and Department of Clinical Chemistry, P.O. Box 60, FIN-00014 University of Helsinki, Finland.) JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY, (2001 Jul) 49 (7) 3178-86. Journal code: 0374755. ISSN: 0021-8561. Pub. country: United States. Language: English.

AB The metabolism of the plant **lignans** matairesinol, secoisolariciresinol, pinoresinol, syringaresinol, arctigenin, 7-**hydroxymatairesinol**, isolariciresinol, and lariciresinol by human fecal microflora was investigated to study their properties as mammalian **lignan** precursors. The quantitative analyses of **lignan** precursors and the mammalian **lignans** enterolactone and enterodiol were performed by HPLC with coulometric electrode array detector. The metabolic products, including mammalian **lignans**, were characterized as trimethylsilyl derivatives by gas chromatography-mass spectrometry. Matairesinol, secoisolariciresinol, lariciresinol, and pinoresinol were converted to mammalian **lignans** only. Several metabolites were isolated and tentatively identified as for syringaresinol and arctigenin in addition to the mammalian **lignans** . Metabolites of 7-**hydroxymatairesinol** were characterized as enterolactone and 7-hydroxyenterolactone by comparison with authentic reference compounds. A metabolic scheme describing the conversion of the most abundant new mammalian **lignan** precursors, pinoresinol and lariciresinol, is presented.

L10 ANSWER 13 OF 53 MEDLINE DUPLICATE 9
2001479553 Document Number: 21414351. PubMed ID: 11522341. alpha,beta-Dibenzyl-gamma-butyrolactone **lignan** alcohols: total synthesis of (+/-)-7'-hydroxyenterolactone, (+/-)-7'-**hydroxymatairesinol** and (+/-)-8-hydroxyenterolactone. Makela T H; Kaltia S A; Wahala K T; Hase T A. (Organic Chemistry Laboratory, Department of Chemistry, P.O. Box 55 (A.I. Virtasen aukio 1), FIN-00014 University of Helsinki, Finland.. taru.makela@helsinki.fi) . STEROIDS, (2001 Oct) 66 (10) 777-84. Journal code: 0404536. ISSN: 0039-128X. Pub. country: United States. Language: English.

AB Two trans-alpha,beta-dibenzyl-gamma-butyrolactone **lignans** carrying a hydroxyl group at the beta-benzylic carbon atom and a alpha-hydroxy alpha,beta-dibenzyl-gamma-butyrolactone **lignan** were synthesized in racemic form using the tandem conjugate addition reaction to construct the basic **lignan** skeleton. Subsequent reaction steps involved either a catalytic reduction of the regenerated keto group to the alcohol, or a hydrogenolysis to benzylic methylene followed by lactone enolate formation and oxidation to give the alpha-hydroxybutyrolactones. These procedures were applied for the synthesis of 7'-hydroxyenterolactones and 7'-**hydroxymatairesinols** , and 8-hydroxyenterolactones, respectively. The diastereomeric mixtures of these compounds were separated either by HPLC techniques or column chromatography and the structures were elucidated using NMR spectroscopy.

L10 ANSWER 14 OF 53 MEDLINE DUPLICATE 10
2002351838 Document Number: 22089888. PubMed ID: 12094633. Uptake and metabolism of **hydroxymatairesinol** in relation to its anticarcinogenicity in DMBA-induced rat mammary carcinoma model. Saarinen N M; Huovinen R; Warri A; Makela S I; Valentin-Blasini L; Needham L; Eckerman C; Collan Y U; Santti R. (Department of Anatomy, Institute of Biomedicine, University of Turku, FIN-20520 Turku, Finland.) NUTRITION AND CANCER, (2001) 41 (1-2) 82-90. Journal code: 7905040. ISSN: 0163-5581. Pub. country: United States. Language: English.

AB The chemopreventive effects of **hydroxymatairesinol** (HMR), a

lignan extracted from Norway spruce (Picea abies), on the development of mammary carcinoma induced by 7,12-dimethylbenz[a]anthracene (DMBA) was studied in rats. HMR administered via diet in an average daily dose of 4.7 mg/kg body wt starting before DMBA induction reduced tumor volume and tumor growth, but no significant reduction in tumor multiplicity (number of tumors/rat) was observed. The predominant histological type in the control group was type B (well-differentiated adenocarcinoma, 78%). The proportion of type B tumors decreased to 35% in the HMR group, while the type A (poorly differentiated) and type C (atrophic) tumor proportions increased. Anticarcinogenic effects of dietary HMR (4.7 mg/kg) were also evident when the administration started after DMBA induction and was seen as growth inhibition of established tumors. Dietary HMR supplementation significantly increased serum and urinary enterolactone and HMR concentrations but had no significant effect on the uterine weight, suggesting that HMR or its major metabolite enterolactone did not have an antiestrogenic effect. Further studies are warranted to further clarify and verify HMR action and the associated mechanisms in mammary tumorigenesis.

L10 ANSWER 15 OF 53 CAPLUS COPYRIGHT 2003 ACS

2000:725669 Document No. 133:286508 **Hydroxymatairesinol** preparations in cancer prevention. Ahotupa, Markku; Eckerman, Christer; Kangas, Lauri; Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni (Hormos Nutraceutical Oy Ltd., Finland). PCT Int. Appl. WO 2000059946 A1 20001012, 43 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-FI181 20000309. PRIORITY: US 1999-281094 19990330.

AB This invention relates to methods for prevention of cancers, certain non-cancer, hormone dependent diseases and/or cardiovascular diseases in a person, based on administering of **hydroxymatairesinol** to said person. The invention also concerns a method for increasing the level of enterolactone or another metabolite of **hydroxymatairesinol** in a person's serum thereby causing prevention of a cancer or a certain non-cancer, hormone dependent disease in a person, based on administering of **hydroxymatairesinol** to said person. Furthermore, this invention relates to pharmaceutical prepns., food additives and food products comprising **hydroxymatairesinol**.

L10 ANSWER 16 OF 53 MEDLINE DUPLICATE 11

2001129080 Document Number: 21016670. PubMed ID: 11130663. Dirigent-mediated podophyllotoxin biosynthesis in Linum flavum and Podophyllum peltatum. Xia Z Q; Costa M A; Proctor J; Davin L B; Lewis N G. (Institute of Biological Chemistry, Washington State University, Pullman 99164-6340, USA.) PHYTOCHEMISTRY, (2000 Nov) 55 (6) 537-49. Journal code: 0151434. ISSN: 0031-9422. Pub. country: United States. Language: English.

AB Given the importance of the antitumor/antiviral **lignans**, podophyllotoxin and 5-methoxypodophyllotoxin, as biotechnological targets, their biosynthetic pathways were investigated in Podophyllum peltatum and Linum flavum. Entry into their pathways was established to occur via dirigent mediated coupling of E-coniferyl alcohol to afford (+)-pinoresinol; the encoding gene was cloned and the recombinant protein subsequently obtained. Radiolabeled substrate studies using partially purified enzyme preparations next revealed (+)-pinoresinol was enantiospecifically converted sequentially into (+)-lariciresinol and (-)-secoisolariciresinol via the action of an NADPH-dependent bifunctional

pinoresinol/lariciresinol reductase. The resulting (-)-secoisolariciresinol was enantiospecifically dehydrogenated into (-)-matairesinol, as evidenced through the conversion of both radio- and stable isotopically labeled secoisolariciresinol into matairesinol, this being catalyzed by the NAD-dependent secoisolariciresinol dehydrogenase. (-)-Matairesinol was further hydroxylated to afford 7'-**hydroxymatairesinol**, this being efficiently metabolized into 5-methoxypodophyllotoxin. Thus much of the overall biosynthetic pathway to podophyllotoxin has been established, that is, from the dirigent mediated coupling of E-coniferyl alcohol to the subsequent conversions leading to 7'-**hydroxymatairesinol**.

L10 ANSWER 17 OF 53 MEDLINE DUPLICATE 12
2001091902 Document Number: 20545126. PubMed ID: 11090976.
Chemopreventive activity of crude hydroxsymatairesinol (HMR) extract in Apc(Min) mice. Oikarinen S I; Pajari A; Mutanen M. (Department of Applied Chemistry and Microbiology (Nutrition), University of Helsinki, P.O. Box 27, FIN-00014, Helsinki, Finland.) CANCER LETTERS, (2000 Dec 20) 161 (2) 253-8. Journal code: 7600053. ISSN: 0304-3835. Pub. country: Ireland. Language: English.

AB We studied the effects of a **lignan, hydroxymatairesinol** (HMR), and rye bran on intestinal tumor development in adenomatous polyposis colimultiple intestinal neoplasia (Apc)(Min) mice. HMR showed a strong chemopreventive effect in this animal model. The mean number of adenomas in the small intestine was significantly lower (26. 6+/-11.0, P<0.05) in mice fed the inulin and HMR when compared with the inulin and inulin/rye bran fed mice (39.6+/-8.9 and 36.0+/-7.4, respectively). HMR resulted in normalization of beta-catenin levels in adenoma tissue, indicating that HMR mediates its chemopreventive effect through the Apc-beta-catenin pathway. In the cytosolic fraction, beta-catenin level in adenoma tissue was significantly elevated (P=0.008-0.013) in all the diet groups as compared with that of the surrounding mucosa. In the nuclear fraction, beta-catenin in the inulin (3.15+/-2.9 relative units) and inulin/rye (5.17+/-6.94 relative units) groups was also significantly higher (P=0.003-0.009) in the adenoma tissue when compared with the surrounding mucosa (0.5+/-0.5 and 0.35+/-0.39 relative units). However, HMR was able to restore nuclear beta-catenin level of the adenoma tissue (0.41+/-0.25 relative units) to the level found in the surrounding mucosa (0.36+/-0.28 relative units).

L10 ANSWER 18 OF 53 SCISEARCH COPYRIGHT 2003 THOMSON ISI
2001:373267 The Genuine Article (R) Number: 428AY. Chemopreventative activity of hydrokysymatairesinol in adenomatous polyposis colimultiple intestinal neoplasia (Apc)(Min) mice (vol 159, pg 183, 2000). Oikannen S I; Pajari A M; Mutanen M (Reprint). Univ Helsinki, Dept Appl Chem & Microbiol Nutr, POB 27, FIN-00014 Helsinki, Finland (Reprint); Univ Helsinki, Dept Appl Chem & Microbiol Nutr, FIN-00014 Helsinki, Finland. CANCER LETTERS (20 DEC 2000) Vol. 161, No. 2, pp. 251-+. Publisher: ELSEVIER SCI IRELAND LTD. CUSTOMER RELATIONS MANAGER, BAY 15, SHANNON INDUSTRIAL ESTATE CO, CLARE, IRELAND. ISSN: 0304-3835. Pub. country: Finland. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We studied the effects of a **lignan, hydroxymatairesinol** (HMR), and rye bran on intestinal tumor development in adenomatous polyposis colimultiple intestinal neoplasia (Apc)(Min) mice. HMR showed a strong chemopreventive effect in this animal model. The mean number of adenomas in the small intestine was significantly lower (26.6 +/- 11.0, P < 0.05) in mice fed the inulin and HMR when compared with the inulin and inulin/rye bran fed mice (39.6 +/- 8.9 and 36.0 +/- 7.4, respectively). HMR resulted in normalization of beta -catenin levels in adenoma tissue, indicating that HMR mediates its chemopreventive effect through the Apc-beta -catenin pathway. In the cytosolic fraction, beta -catenin level. in adenoma tissue was

significantly elevated (P = 0.008-0.013) in all the diet groups as compared with that of the surrounding mucosa. In the nuclear fraction, beta -catenin in the inulin (3.15 +/- 2.9 relative units) and inulin/rye (5.17 +/- 6.94 relative units) groups was also significantly higher (P = 0.003-0.009) in the adenoma tissue when compared with the surrounding mucosa(0.5 +/- 0.5 and 0.35 +/- 0.39 relative units). However, HMR was able to restore nuclear beta -catenin level of the adenoma tissue (0.41 +/- 0.25 relative units) to the level found in the surrounding mucosa (0.36 +/- 0.28 relative units). (C) 2000 Published by Elsevier Science Ireland Ltd. All rights reserved.

L10 ANSWER 19 OF 53 MEDLINE DUPLICATE 13
2001103469 Document Number: 20348508. PubMed ID: 10890032.
Hydroxymatairesinol, a novel enterolactone precursor with antitumor properties from coniferous tree (Picea abies). Saarinen N M; Warri A; Makela S I; Eckerman C; Reunanen M; Ahotupa M; Salmi S M; Franke A A; Kangas L; Santti R. (Department of Anatomy, University of Turku, Finland.) NUTRITION AND CANCER, (2000) 36 (2) 207-16. Journal code: 7905040. ISSN: 0163-5581. Pub. country: United States. Language: English.

AB The potential for the extraction of the plant **lignan** **hydroxymatairesinol** (HMR) in large scale from Norway spruce (Picea abies) has given us the opportunity to study the metabolism and biological actions of HMR in animals. HMR, the most abundant single component of spruce **lignans**, was metabolized to enterolactone (ENL) as the major metabolite in rats after oral administration. The amounts of urinary ENL increased with the dose of HMR (from 3 to 50 mg/kg), and only minor amounts of unmetabolized HMR isomers and other **lignans** were found in urine. HMR (15 mg/kg body wt po) given for 51 days decreased the number of growing tumors and increased the proportion of regressing and stabilized tumors in the rat dimethylbenz[a]anthracene-induced mammary tumor model. HMR (50 mg/kg body wt) did not exert estrogenic or antiestrogenic activity in the uterine growth test in immature rats. HMR also showed no antiandrogenic responses in the growth of accessory sex glands in adult male rats. Neither ENL nor enterodiol showed estrogenic or antiestrogenic activity via a classical alpha- or beta-type estrogen receptor-mediated pathway in vitro at < 1.0 microM. HMR was an effective antioxidant in vitro.

L10 ANSWER 20 OF 53 MEDLINE DUPLICATE 14
2001029197 Document Number: 20452988. PubMed ID: 10996730.
Chemopreventative activity of crude **hydroxymatairesinol** (HMR) extract in Apc(Min) mice [corrected]. Oikannen S I; Pajari A M; Mutanen M. (Department of Applied Chemistry and Microbiology (Nutrition), University of Helsinki, P.O. Box 27, FIN-00014, Helsinki, Finland.) CANCER LETTERS, (2000 Oct 31) 159 (2) 183-7. Journal code: 7600053. ISSN: 0304-3835. Pub. country: Ireland. Language: English.

AB We studied the effects of a **lignan, hydroxymatairesinol** (HMR), and rye bran on intestinal tumor development in adenomatous polyposis colimultiple intestinal neoplasia (Apc)(Min) mice. HMR showed a strong chemopreventive effect in this animal model. The mean number of adenomas in the small intestine was significantly lower (26.6+/-11.0, P<0.05) in mice fed the TNS tumor promoter insulin and HMR when compared with the insulin and insulin/rye bran fed mice (39.6+/-8.9 and 36.0+/-7.4, respectively). HMR resulted in normalization of beta-catenin levels in adenoma tissue, indicating that HMR mediates its chemopreventive effect through the Apc-beta-catenin pathway. In the cytosolic fraction, beta-catenin level in adenoma tissue was significantly elevated (P=0.008-0.013) in all the diet groups as compared with that of the surrounding mucosa. In the nuclear fraction, beta-catenin in the insulin (3.15+/-2.9 relative units) and insulin/rye (5.17+/-6.94 relative units) groups was also significantly higher (P=0.003-0.009) in the adenoma tissue when compared with the surrounding mucosa (0.5+/-0.5 and 0.35+/-0.39

Chamaecyparis formosensis. These components include 18 sesquiterpenes, 40 diterpenes, 8 flavones, 7 **lignans** and 11 misc. compds. Among them 3 sesquiterpenes, 7 diterpenes and one **lignan** are new compds., the structures of which were detd. by chem. and spectral methods.

L10 ANSWER 24 OF 53 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 16

2000:11602 Document No.: PREV200000011602. Antioxidative **lignans** from industrial wastewater in cleaning of black sesame seed. Nagashima, Mayumi (1); Fukuda, Yasuko; Ito, Ryuhei. (1) Ichimura Gakuen College, 61-1 Uchikubo, Inuyama-shi, Aichi, 484-8503 Japan. Nippon Shokuhin Kagaku Kogaku Kaishi, (1999) Vol. 46, No. 6, pp. 382-388. ISSN: 1341-027X. Language: Japanese. Summary Language: English; Japanese.

AB The increase in industrial waste is one of the serious social problems. In this respect, we have searched for any useful materials from wastewater in cleaning of black sesame seed, one of food industrial wastes. In this paper, we describe the isolation, the structural elucidation and the antioxidative activity of four **lignans**, compounds 1apprx4, from the wastewater and on HPLC analysis of water extracts of black sesame seed coat and white sesame seed coat. Compounds 1apprx4 were isolated by column chromatography and preparative HPLC. On the basis of spectroscopic evidence, compounds 1apprx4 were respectively identified as pinoresinol, larisiresinol, **hydroxymatairesinol**, allohydroxymatairesinol. Compounds 2, 3, 4 have not been detected in sesame seed. On antioxidative activity by the thiocyanate method with AAPH, compounds 1apprx4 showed the weaker activities than BHT. On the DPPH radical-scavenging activities by a colorimetric method, compound 3 was as effective as alpha-tocopherol, and compound 4 showed the stronger activity than alpha-tocopherol. By HPLC analysis, it was ascertained that compounds 1apprx4 were not artifacts but were originally present in black sesame seed coat, in addition, it was proved that the content of compounds 1 and 2 in black sesame seed coat was four times more than that in white sesame seed coat.

L10 ANSWER 25 OF 53 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 17

1998:765235 The Genuine Article (R) Number: 124WQ. NMR-spectroscopic study of **hydroxymatairesinol**, the major **lignan** in Norway spruce (Picea abies) heartwood. Mattinen J (Reprint); Sjoholm R; Ekman R. ABO AKAD UNIV, DEPT ORGAN CHEM, FIN-20500 TURKU, FINLAND (Reprint); ABO AKAD UNIV, LAB FOREST PROD CHEM, FIN-20500 TURKU, FINLAND. ACH-MODELS IN CHEMISTRY (21 SEP 1998) Vol. 135, No. 4, pp. 583-590. Publisher: AKADEMIAI KIADO. PO BOX 245, H-1519 BUDAPEST, HUNGARY. ISSN: 1217-8969. Pub. country: FINLAND. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The heartwood **lignans** of Norway spruce (Picea abies) were isolated by solvent extraction. **Hydroxymatairesinol**, the dominant **lignan** and its major isomer (weight ratio 3.5:1) were separated by preparative TLC and their structures were elucidated using NMR spectroscopy and molecular modelling.

L10 ANSWER 26 OF 53 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 18

1999:59436 The Genuine Article (R) Number: 154PE. Photodiscoloration of western hemlock (Tsuga heterophylla) sapwood - III - Early stage of photodiscoloration reaction with **lignans**. Kawamura F (Reprint); Miyachi M; Kawai S; Ohashi H. AKITA PREFECTURAL COLL AGR, INST WOOD TECHNOL, NOSHIRO 016, JAPAN (Reprint); GIFU UNIV, UNITED GRAD SCH AGR SCI, GIFU 50111, JAPAN; GIFU UNIV, FAC AGR, GIFU 50111, JAPAN. JOURNAL OF WOOD SCIENCE (JUN 1998) Vol. 44, No. 1, pp. 47-55. Publisher: SPRINGER-VERLAG TOKYO. 3-3-13, HONGO, BUNKYO-KU, TOKYO 113, JAPAN. ISSN: 1435-0211. Pub. country: JAPAN. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The reaction during the early stage of photodiscoloration of constituents in western hemlock [Tsuga heterophylla (Raf.) Sarg.,

Pinaceae] sapwood was investigated with chemical methods. The main photodiscoloring constituents, **hydroxymatairesinol**, allohydroxymatairesinol, alpha-conidendrin, and oxomatairesinol, were used as substrates for light-irradiation experiments in vitro. The structures of photodiscoloration reaction products were elucidated by isolation and instrumental analyses and/or co-high-performance liquid chromatography analyses with authentic specimens. The experiment was undertaken to distinguish each series of liquid phases using chloroform, water (both including a trace of methanol), and methanol, and the solid phase. The reaction products allohydroxymatairesinol (2), oxomatairesinol (3), alpha-conidendrin (4), allo-7'-methoxymatairesinol (5), 7'-methoxymatairesinol (6), and vanillin (7) were isolated or detected in the reaction mixture of a **hydroxymatairesinol** system. The reaction products **hydroxymatairesinol** (1), 3, 4, 5, 6, and 7 were confirmed in the reaction system of allohydroxymatairesinol, which was an epimer of **hydroxymatairesinol**. Product 3 was confirmed from the alpha-conidendrin system, and reaction product 7 was confirmed from oxomatairesinol. The photodiscoloration reaction of western hemlock sapwood could be initiated by the formation of phenoxy radicals from the respective constituents. The reaction was then presumed to progress via formation of a quinonemethide intermediate in many of them. Tt was suggested that the reactive species, such as phenoxy radical or quinonemethide intermediate, formed by light-irradiation might be converted to quinone derivatives and colored oligomers. Products 1, 2, 3, 4, and 7, formed from substrates such as **hydroxymatairesinol**, allohydroxymatairesinol, alpha-conidendrin, and oxomatairesinol, were the same as the original metabolic constituents of western hemlock. Therefore it was concluded that the photodiscoloration of western hemlock depends not on the quantitative level of a few respective metabolites but, rather, on the coexistence of many metabolites.

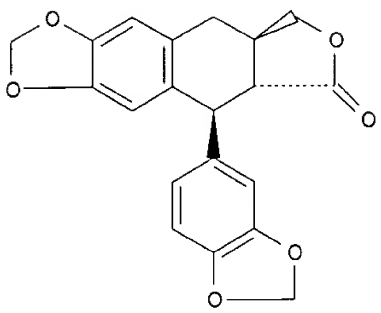
L10 ANSWER 27 OF 53 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 19
96:359728 The Genuine Article (R) Number: UH886. PHOTODISCOLORATION OF WESTERN HEMLOCK (TSUGA-HETEROPHYLLA) SAPWOOD .2. STRUCTURES OF CONSTITUENTS CAUSING PHOTODISCOLORATION. KAWAMURA F (Reprint); OHASHI H; KAWAI S; TERATANI F; KAI Y. GIFU UNIV, UNITED GRAD SCH AGR SCI, GIFU 50111, JAPAN (Reprint). MOKUZAI GAKKAISHI (1996) Vol. 42, No. 3, pp. 301-307. ISSN: 0021-4795. Pub. country: JAPAN. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The constituents causing photodiscoloration in Tsuga heterophylla (Raf.) Sarg. (Western hemlock, Pinaceae) sapwood were investigated. Five **lignans** and one neolignan, the main constituents causing the discoloration, were isolated from the ethyl acetate soluble fraction of the methanol extract of sapwood powders. (+)-Cedrusin (1), (+)-allohydroxymatairesinol (2), (-)-**hydroxymatairesinol** (3), (+)-oxomatairesinol (4), (-)-alpha-conidendrin (5) and (+)-Pinoresinol (6) were determined or identified by instrumental analysis The constituents (1)-(3), the assignment of proton and carbon atoms corrected by a series of NMR analyses, or their stereochemical configurations finally were solved. In addition, Vanillic acid (7), catechin (8) and vanillin (9) were detected as minor constituents causing the discoloration by co-TLC and/or HPLC with authentic specimens. Almost all of them were found to contain two common structure moieties, a guaiacyl ring structure and an oxigenation structure, at the neighboring alpha-position on the aromatic ring, which might be presumed to cause the photodiscoloration of western hemlock sapwood.

L10 ANSWER 28 OF 53 CAPLUS COPYRIGHT 2003 ACS
1995:133154 Document No. 122:76524 Cytotoxic **lignans** from Haplophyllum species. Ulubelen, A.; Gil, R. R.; Cordell, G. A.; Mericli, A. H.; Mericli, F. (Fac. Pharmacy, Univ. Istanbul, Istanbul, 34452, Turk.). Pure and Applied Chemistry, 66(10/11), 2379-82 (English) 1994.

CODEN: PACHAS. ISSN: 0033-4545.

GI



I

AB Four new **lignans**: 1.beta.-polygamain, (I), 4-isopentylhaplomyrfolin Type A and B, and 4-geranoyl-9-**hydroxymatairesinol**, were isolated from Haplophyllum ptilostylum, their structures were established by spectral data, using COSY, HETCOR, COLOC, selective INEPT expts. Pharmacol. tests were performed on human cell lines and HIV-1 reverse transcriptase.

L10 ANSWER 29 OF 53 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 20

94:740582 The Genuine Article (R) Number: PR974. THE EXTRACTIVES OF AOMORI TODOMATSU (ABIES-MARIESII MASTERS) - ISOLATIONS OF **LIGNANS** FROM THE HEARTWOOD. OMORI S (Reprint); OZAWA S; TANEDA K. SUNY SYRACUSE, COLL ENVIRONM SCI & FORESTRY, SYRACUSE, NY, 13210 (Reprint); IWATE UNIV, FAC AGR, MORIOKA, IWATE 020, JAPAN. MOKUZAI GAKKAISHI (1994) Vol. 40, No. 10, pp. 1107-1118. ISSN: 0021-4795. Pub. country: USA; JAPAN. Language: Japanese.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB This study examined the extractive components of Abies mariesii Masters (Aomori todomatsu). This hardy softwood species is grown primarily in the coldest region of the main island of Japan.

The ether and hexane soluble extractives from the heartwood of A. mariesii were determined. Ten compounds were identified from ether soluble fractions: alpha-conidendrin (I), matairesinol (II), ketomatairesinol (III), **hydroxymatairesinol** (IV), 1,2,3,4-tetrahydro-7-hydroxy-r-1-(4'-hydroxy-3'-methoxyphenyl)-t-2-hydroxymethyl-6-methoxy-c-3-naphthalenecarbaldehyde gamma-lactol (todolactol-B, V), t-4-(4'-hydroxy-3'-methoxybenzoyl)-r-2-(4''-hydroxy-3''-methoxyphenyl)-t-3-hydroxymethyl-tetrahydrofuran (VI), 2-hydroxy-t-4-[hydroxy(4'-hydroxy-3'-methoxyphenyl)methyl]-r-3- (4''-hydroxy-3''-methoxybenzyl)-tetrahydrofuran (todolactol-A, VII), t-4-(p-coumaroyloxy) (4'-hydroxy-3'-methoxyphenyl)methyl-2-hydroxy-r-3-(4''-hydroxy-3''-methoxybenzyl)-tetrahydrofuran (todolactol-A alpha'-p-coumarate, VIII),vanillic acid (IX),and t-4-[hydroxy (4'-hydroxy-3'-methoxyphenyl)methyl]-r-2-(4''-hydroxy-3''-methoxyphenyl)-t-3-hydroxymethyl-tetrahydrofuran (X), and beta-sitosterol (XI) was isolated and identified from the hexane soluble fraction. In this study the major features were a relatively large yield of matairesinol (II), comparable to that of compounds alpha-conidendrin (I) and **hydroxymatairesinol** (IV), and the presence of the lactol-type phenolic **lignans** such as Compounds (V), (VII), and (VIII).

L10 ANSWER 30 OF 53 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 21

94211290 EMBASE Document No.: 1994211290. Taxoids from the roots of Taxus x medica cv. Hicksii. Appendino G.; Cravotto G.; Enriu R.; Gariboldi P.; Barboni L.; Torregiani E.; et al.. Dipt. Scienza/Tecnologia del Farmaco,

via Giuria 9,10125 Torino, Italy. Journal of Natural Products 57/5 (607-613) 1994.
ISSN: 0163-3864. CODEN: JNPRDF. Pub. Country: United States. Language: English. Summary Language: English.

AB The roots of Taxus x media cv. Hicksii gave two new pseudoalkaloidal taxoids, identified as N-debenzoyl-N-butanoyl taxol [1] and 7.beta.-acetoxy-9- acetylspicataxine [2a]. A new baccatin IV derivative [7a] and the **lignans hydroxymatairesinol** [8] and (-)-epinortrachelogenin [9] were also isolated. The epoxidation of .DELTA.(4(20),11) taxadienes was investigated, disclosing an unusual reactivity of the bridgehead double-bond towards peracids. Regiochemically and stereochemically unnatural epoxides of taxoids were obtained. Nmr data for these compounds were compared with literature values on the natural epoxides. No significant correlation between the configuration of the 4(20)-oxirane ring and the chemical shift of H-5 was found.

L10 ANSWER 31 OF 53 CAPLUS COPYRIGHT 2003 ACS

1990:79734 Document No. 112:79734 The wood extractives in alkaline peroxide bleaching of groundwood from Norway spruce. Ekman, Rainer; Holmbom, Bjarne (Lab. For. Prod. Chem., Abo Akad., Abo, SF-20500, Finland). Nordic Pulp & Paper Research Journal, 4(3), 188-91 (English) 1989. CODEN: NPPJEG. ISSN: 0283-2631.

AB The changes in extractive compn. of groundwood pulp from Norway spruce upon alk. H2O2 bleaching in a paper mill were investigated by gas chromatog. Only slight hydrolysis of esterified fatty acids occurred in bleaching and no significant alteration of the compn. of the fatty acids was obsd. No changes were found in the amt. and compn. of free and esterified sterols. However, considerable oxidn. of abietadienoic resin acids occurred whereas the pimaric-type resin acids and dehydroabietic acid were practically unaffected by bleaching. Among the polar extractives, the spruce **lignans** exhibited a drastic decrease including alkali-induced transformation of **hydroxymatairesinol** to conidendric acid. The spruce bark derived stilbenes were almost completely oxidized in bleaching. Alk. H2O2 bleaching produced a series of aliph. C2-C4 hydroxy and dicarboxylic acids. Glycolic, oxalic, 2-deoxytetronic and malic acids were the major components of this group.

L10 ANSWER 32 OF 53 CAPLUS COPYRIGHT 2003 ACS

1989:121412 Document No. 110:121412 Pharmaceuticals containing leucoanthocyans for the treatment of alcoholism. Brekhman, I. I.; Bulanov, A. E.; Polozhentseva, M. I.; Mudzhiri, L. A.; Alkhazashvili, G. G.; Kalatozishvili, E. I.; Dardymov, I. V.; Bezdetko, G. N.; Khasina, E. I. (Institute of Biology of the Sea, Vladivostok, USSR; Scientific-Research Institute of Horticulture, Viticulture, and Wine Making). Ger. Offen. DE 3641495 A1 19880609, 21 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1986-3641495 19861204.

AB A pharmaceutical for the treatment of pathol. alc. addiction contains leucoanthocyans 219-270, catechins 153-187, flavonols 81-99, lignin 68-83, reducing saccharides 216-264, pectin 18-22, free amino acids 27-33, org. acids 36-44, sterols 4.5-5.5, methylsterols 1.35-1.65, dimethylsterols 1.98-2.42, **lignans** 13.5-16.5, **lignan** glycosides 9-11, phenolcarboxylic acids 13.5-16.5, phenolaldehydes 4.5-5.5, and alkyl ferulates 4.5-5.5 mg/g. Alc. rats received drinking water contg. 15% EtOH and 1 mL/50 mL of the above mixt. for 13 wk and were then kept abstinent for 10 days; in the abstinent animals the deprivation occurred without alc. withdrawal symptoms. Animals receiving the above mixt. and free to choose water or 15% EtOH-contg. water, decreased their EtOH consumption by 100% after the deprivation period, whereas alc. consumption increased in the control.

L10 ANSWER 33 OF 53 CAPLUS COPYRIGHT 2003 ACS

1985:593134 Document No. 103:193134 A study of the constituents of the

heartwood of Tsuga chinensis Pritz. var. formosana (Hay.). Fang, Jim Min; Wei, Kuo Min; Cheng, Yu Shia (Dep. Chem., Natl. Taiwan Univ., Taipei, Taiwan). Journal of the Chinese Chemical Society (Taipei, Taiwan), 32(1), 75-80 (English) 1985. CODEN: JCCTAC. ISSN: 0009-4536.

AB By means of spectroscopic anal., x-ray crystallog., and chem. correlation the heartwood of Taiwan hemlock was found to contain sterols, carboxylic acids, 13-epimanool, o-methoxyphenolics, coniferaldehyde, benzofuranoid neolignan, .alpha.-conidendrin, tsugacetal, isolariciresinol, secoisolariciresinol, matairesinol, **hydroxymatairesinol** and oxomatairesinol. Among them (+)-tsugacetal is a novel **lignan** acetal having an .alpha.-conidendrin-related structure with the acetal methoxy group at the .beta.-position.

L10 ANSWER 34 OF 53 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 22

1982:255084 Document No.: BA74:27564. **LIGNANS** FROM TAXUS-WALLICHIANA. MILLER R W; MCLAUGHLIN J L; POWELL R G; PLATTNER R D; WEISLEDER D; SMITH C R. NORTH REG. RES. CENT., AGRIC. RES. SERV., US DEP. AGRIC., PEORIA, ILL. 61604.. J NAT PROD (LLOYDIA), (1982) 45 (1), 78-82. CODEN: JNPRDF. ISSN: 0163-3864. Language: English.

AB Three **lignans** were isolated from the roots, stems and needles of T. wallichiana Zucc. Two of these were identified as epimers of conidendrin and **hydroxymatairesinol**. The structure of the 3rd, a previously unknown **lignan** named isoliovil, was established by 1H and 13C NMR and mass spectrometry.

L10 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS

1982:102372 Document No. 96:102372 Spectrophotometric determination of **lignans** in oakwood and brandy spirits. Kuridze, M. G.; Leont'eva, V. G.; Mudzhiri, L. A.; Semenov, A. A.; Lashkhi, A. D. (Nauchno-Issled. Inst. Sadovod., Vinograd. Vinodel., Tbilisi, USSR). Izvestiya Akademii Nauk Gruzinskoi SSR, Seriya Khimicheskaya, 7(3), 213-23 (Russian) 1981. CODEN: IGSKDH. ISSN: 0132-6074.

AB To det. lignin [9005-53-2] components, a sample (100 mL brandy or alc. ext. of oak wood) is concd., purified by column chromatog. on Chromaton N-AW, and resolved by TLC on silica gel. The individual components (secoisolariciresinol [29388-59-8], liovil [484-39-9], lariciresinol [27003-73-2], olivil [2955-23-9], pinoresinol [487-36-5], eudesmin [526-06-7], matairesinol [580-72-3], **hydroxymatairesinol** [20268-71-7], and isolariciresinol [548-29-8]) are sep. eluted with EtOH and the optical d. of each soln. is measured in a spectrophotometer (SF-26) at the appropriate wavelength in the UV region. The amt. of lignin component is computed from a calibration curve. The relative error of the method was .ltoreq.1.88%. The total lignin content in brandy increased upon storage from 41.4 mg/L (after 1 yr) to 140.9 mg/mL (after 20 yr).

L10 ANSWER 36 OF 53 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

1982:189604 Document No.: BA73:49588. **LIGNANS** IN EASTERN HEMLOCK TSUGA-CANADENSIS. NAVAS S M; OMORI S. DEP. DE MADERAS, INST. TECNOL. DE COSTA RICA, APARTADO 159, CARTAGO, COSTA RICA A.C.. BULL IWATE UNIV FOR, (1981) 0 (12), 29-89. CODEN: IDNEAI. Language: English.

AB Comparisons of the chloroform-soluble extract components of eastern hemlock using standards from combined column chromatography, TLC and reverse phase high-pressure liquid chromatography [HPLC] techniques indicated the presence of the **lignans** pinoresinol, pinoresinol methyl ether, pinoresinol dimethyl ether, syringaresinol, conidendrin, matairesinol, oxomatairesinol, **hydroxymatairesinol**, liovil and isolariciresinol. Only conidendrin had been previously reported in eastern hemlock (Erdtman, 1944). .alpha.- and .beta.-Conidrendrol were not present in the heartwood chloroform-soluble extract. Although open column elution chromatography is a useful technique for the partial separation of natural

mixtures of **lignans**, it is not adequate for the isolation of pure **lignans**. Silica gel or cellulose TLC was a good method for identification of **lignans**. The use of reverse phase HPLC in the analysis of **lignans** was not previously reported. Reverse phase HPLC is a sensitive and rapid method for the separation of **lignans** . Pinoresinol and conidendrin, e.g., were separable by reverse phase HPLC but were not readily separable by silica gel TLC. There were instances in which the technique could not distinguish between separate **lignans** . The following pairs of standards could not be separated: liovil and and **hydroxymatairesinol**, .alpha.-conidendrin and matairesinol, and pinoresinol and syringaresinol. The system was inadequate for the separation of liovil, **hydroxymatairesinol** and isolarioiresinol in natural mixtures. The reverse phase HPLC method is both rapid and relatively easy to use. Most of the peaks of the chromatograms were produced within 15 min of injection of the **lignan**-containing samples. The preparation of derivatives was unnecessary since pure compounds or mixtures can be injected into the chromatograph in their natural state.

L10 ANSWER 37 OF 53 CAPLUS COPYRIGHT 2003 ACS
1982:102368 Document No. 96:102368 Lignane in oak wood and cognac alcohols. Kuridze, M. G.; Mudzhiri, L. A.; Lashkhi, A. D.; Leont'eva, V. G.; Semenov, A. A. (Nauchno-Issled. Inst. Sadovod. Vinograd. Vinodel., Tbilisi, USSR). Vinodelie i Vinogradarstvo SSSR (8), 12-14 (Russian) 1981. CODEN: VIVSA6. ISSN: 0042-6318.

AB A method is described for detg. lignin substances in oak wood and cognac, based on extn. with org. solvents (acetone, CHCl3-MeOH, C6H6-EtOAc, and CHCl3-acetone), followed by TLC on silica gel and spectrophotometry. Nine lignin substances were identified: secoisolariciresinol [29388-59-8], liovil [484-39-9], lariciresinol [27003-73-2], olivil [2955-23-9], pinoresinol [487-36-5], eudesmin [526-06-7], matairesinol [580-72-3], **hydroxymatairesinol** [20268-71-7], and isolariciresinol [548-29-8]. The contents of each of these substances in wine increased significantly upon prolonged storage from 4.5 mg/mL (after 1 yr) to 16 mg/mL (after 20 yr).

L10 ANSWER 38 OF 53 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
1981:171146 Document No.: BA71:41138. A DEGRADED **LIGNAN** FROM ALKALINE HYDROLYSIS OF NORWAY SPRUCE PICEA-ABIES ROOT EXTRACTIVES. EKMAN R; SJOHOLM R T; SJOHOLM R. INST. WOOD CHEM. CELL. TECH., ABO AKADEMI, SF-20500 ABO 50, FINL.. FINN CHEM LETT, (1979) 0 (4), 126-128. CODEN: FCMLAS. ISSN: 0303-4100. Language: English.

AB Analysis of alkali-treated phenolic extractives from Norway spruce rootwood revealed the presence of (E)-4-(4-hydroxy-3-methoxyphenyl)-2-(4-hydroxy-3-methoxyphenylmethyl)but-3-enoic acid (1). This compound, which was also detected in the neutralized kraft black liquor from pulping of unextracted spruce rootwood, is derived from the **lignan** **hydroxymatairesinol**. In pilot-plant experiments designed for the isolation of spruce extractives prior to pulping, the yield of 1 was about 3 g/kg dry rootwood.

L10 ANSWER 39 OF 53 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
1978:192745 Document No.: BA66:5242. O ACYL DERIVATIVE **LIGNANS** FROM WOOD OF THE GENUS ABIES. LEONT'EVA V G; MODONOVA L D; TYUKAVKINA N A; PUNTUSOVA E G. IRKUTSK INST. ORG. CHEM., SIB. DEP., ACAD. SCI. USSR, IRKUTSK, USSR.. KHIM PRIR SOEDIN (TASHK), (1977 (RECD 1978)) (3), 337-341. CODEN: KPSUAR. ISSN: 0023-1150. Language: Russian.

AB Five new compounds were chromatographically isolated from the wood of A. sibirica and A. nephrolepis. These proved to be complex esters derivatives of the **lignans** lariciresinol, olivil and **hydroxymatairesinol**. Their structure was analyzed on the basis of spectroscopic data.

L10 ANSWER 40 OF 53 CAPLUS COPYRIGHT 2003 ACS
1978:71443 Document No. 88:71443 **Lignan** compounds in the needles of some species of the Pinaceae family. Tyukavkina, N. A.; Medvedeva, S. A.; Ivanova, S. Z.; Lutskii, V. I. (Inst. Org. Khim., Irkutsk, USSR). Koksnes Kimija (6), 94-6 (Russian) 1977. CODEN: KHDRDQ. ISSN: 0201-7474.
AB Of the **lignans** extd. from needles of fir, spruce, larch, and pine species, secoisolariciresinol was present in all species, except those of fir; liovil, lariciresinol, matairesinol, and isolariciresinol were found in all species, olivil was absent in fir species, Picea ajanensis, and Larix sibirica; pinoresinol was absent in Abies sibirica and L. sibirica; **hydroxymatairesinol** was found only in spruce species; ketomatairesinol trace amts. were detected in P. koreansis only; and .alpha.-conidendrin was found in trace amts. in L. dahurica only. The total **lignan** content of needles was 0.03-0.09% (on dry-wt. basis). The needles did not contain 3,4-divanillyltetrahydrofuran, which is normally present in wood.

L10 ANSWER 41 OF 53 CAPLUS COPYRIGHT 2003 ACS
1976:556276 Document No. 85:156276 Effect of spruce root constituents on extracellular enzymes of Fomes annosus. Johansson, Martin; Popoff, Thomas; Theander, Olof (Dep. Forest Bot. Pathol., R. Coll. For., Stockholm, Swed.). Physiologia Plantarum, 37(4), 275-82 (English) 1976. CODEN: PHPLAI. ISSN: 0031-9317.
AB Investigations were carried out to study the effects of fractionated Me2CO exts. and purified compds. from spruce roots on cellulase, polygalacturonase, aryl-.beta.-glucosidase, and laccase produced by a strain of F. annosus. The presence of active laccase in a hydrolyzing enzyme prepn. resulted in increased enzyme inhibition, esp. by fractions from the reaction zones. In expts. to det. the effect of predominant **lignans** in the reaction zone, viz. **hydroxymatairesinol**, on the enzymes with and without previous oxidn. by laccase, aryl-.beta.-glucosidase was esp. inhibited by the oxidized **lignan**. Polygalacturonase was inhibited by all light petroleum fractions (resins and fatty acids), while aryl-.beta.-glucosidase was not. In expts. in which the 4 extracellular enzymes were treated with 7 of the 9 fractions contained in the butanone phase of the Me2CO ext. from the reaction zone, all of the enzymes were inhibited by partly different **lignan** fractions, while phenolic fractions weakly inhibited the biosynthesis of the enzymes.

L10 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2003 ACS
1976:474919 Document No. 85:74919 Analysis of **lignans** in Norway Spruce by combined gas chromatography-mass spectrometry. Ekman, Rainer (Inst. Wood Chem. Cellul. Technol., Abo Akad., Abo, Finland). Holzforschung, 30(3), 79-85 (English) 1976. CODEN: HOLZAZ. ISSN: 0018-3830.
AB Me2CO-sol. **lignans** of spruce wood contained 0.5% guiaiacyl type **lignans**. The compds. identified in the ext. were isolariciresinol, secoisolariciresinol, liovil, .alpha.-conidendric acid, **lignan** A and B, lariciresinol, 2 **hydroxymatairesinol** isomers, pinoresinol, matairesinol, and .alpha.-conidendrin. Six unidentified **lignans** of the tetrahydrofuran series were also detected.

L10 ANSWER 43 OF 53 CAPLUS COPYRIGHT 2003 ACS
1975:544638 Document No. 83:144638 Changes in sapwood of roots of Norway spruce, attacked by Fomes annosus. II. Organic chemical constituents and their biological effects. Popoff, Thomas; Theander, Olof; Johansson, Martin (Dep. Chem., Swed. For. Prod. Res. Lab., Stockholm, Swed.). Physiologia Plantarum, 34(4), 347-56 (English) 1975. CODEN: PHPLAI. ISSN: 0031-9317.

AB Acetone exts. of sapwood and reaction zone of spruce roots attacked by F. annosus, collected in February, June, and October, were sepd. into resinous and phenolic fractions. The fractions were further sepd. by column, thin layer, and gas liq. chromatog., followed by biol. tests, using F. annosus and other rot fungi. The reaction zone contained quant. less light petroleum sol. compds. than the sapwood but more acids. The phenolic content was about ten times higher in the reaction zone than in the sapwood. Nine **lignans** and 1 simple phenol (4-methylcatechol) were identified and quant. estd. in the reaction zone. The resinous fraction of the ext. from the reaction zone as well as some of the **lignans** and 4-methylcatechol inhibited fungal growth, in some cases followed by detoxification and continued growth. The predominant **lignan, hydroxymatairesinol,** had no effect on F. annosus or 5 other wood degrading fungi. About 15 unidentified phenols were obsd., some of them probably of importance as inhibitors, either alone or in combination with other phenols.

L10 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2003 ACS
1974:532858 Document No. 81:132858 **Lignans** from Picea koraiensis wood. Leont'eva, V. G.; Modonova, L. D.; Tyukavkina, N. A. (Irkutsk. Inst. Org. Khim., Irkutsk, USSR). Khimiya Prirodnykh Soedinenii (3), 399-400 (Russian) 1974. CODEN: KPSUAR. ISSN: 0023-1150.
AB **Lignan** contents (3,4-divanillyltetrahydrofuran, liovil, lariciresinol, pinoresinol, ketomatairesinol, matairesinol, **hydroxymatairesinol,** isolariciresinol, .alpha.-conidendrin, and vanillin) in P. koraiensis, P. obovata, and P. ajanensis are tabulated. P. ajanensis contained more cyclic **lignans** than the other 2.

L10 ANSWER 45 OF 53 CAPLUS COPYRIGHT 2003 ACS
1974:548518 Document No. 81:148518 **Lignans** from Abies sibirica wood. Leont'eva, V. G.; Modonova, L. D.; Tyukavkina, N. A. (Irkutsk. Inst. Org. Khim., Irkutsk, USSR). Izvestiya Sibirskogo Otdeleniya Akademii Nauk SSSR, Seriya Khimicheskikh Nauk (4), 158-61 (Russian) 1974. CODEN: IZSKAB. ISSN: 0002-3426.
AB The acetonic ext. fraction insol. in ligroin contained secoisolariciresinol (I), 3,4-divanilyltetrahydrofuran (II), liovil (III), lariciresinol (IV), pinoresinol (V), olivil, matairesinol, and **hydroxymatairesinol**. Of these, I-V were detd. for the 1st time in the wood of the Abies genus.

L10 ANSWER 46 OF 53 CAPLUS COPYRIGHT 2003 ACS
1975:141811 Document No. 82:141811 **Lignan** compounds of Siberian spruce wood (Picea obovata). Modonova, L. D.; Tyukavkina, N. A. (Irkutsk. Inst. Org. Khim., Irkutsk, USSR). Khim. Ispol'z. Lignina, 73-86. Editor(s): Sergeev, V. N. "Zinatne": Riga, USSR. (Russian) 1974. CODEN: 29THA7.
AB The extn. of Picea obovata with MeOH or acetone gave 8.8 or 8.7% (on dry wood wt.) resp. of phenolic constituents. These compds. were sepd. by thin layer chromatog. and identified as conidendrin [518-55-8], 3,4-divanillyltetrahydrofuran [34730-78-4], pinoresinol [487-36-5], matairesinol [580-72-3], ketomatairesinol [53250-61-6], lariciresinol [27003-73-2], **hydroxymatairesinol** [20268-71-7], and liovil [484-39-9]. The wood of Picea obovata had low resistance to fungus infection. Biol. testing showed that none of the above-indicated **lignans** had any fungicidal properties.

L10 ANSWER 47 OF 53 CAPLUS COPYRIGHT 2003 ACS
1975:74652 Document No. 82:74652 **Lignans** from Abies nephrolepis and Picea ajanensis. Leont'eva, V. G.; Modonova, L. D.; Tyukovkina, N. A. (Irkutsk. Inst. Org. Khim., Irkutsk, USSR). Khimiya Prirodnykh Soedinenii (2), 268-9 (Russian) 1973. CODEN: KPSUAR. ISSN: 0023-1150.
AB The phenolic substances, extd. from Picea ajanensis with acetone, include

.alpha.-conidendrin [518-55-8], matairesinol (I) [580-72-3], ketomatairesinol, **hydroxymatairesinol** (II) 3,4-divinyltetrahydrofuran (III) [41233-91-4], (+)-pinoresinol (IV) [487-36-5], liovil (V) [484-39-9], isolariciresinol [548-29-8], vanillin (VI) [121-33-5], and vanillic acid [121-34-6]. The exts. from Abies nephrolepis contain I-VI. The substances were sepd. by chromatog. on powd. polyamide and silica gel impregnated with 2% Na metabisulfite soln.

L10 ANSWER 48 OF 53 CAPLUS COPYRIGHT 2003 ACS
1973:99363 Document No. 78:99363 Isolation of two **lignans** from Ezomatsu (Picea jezoensis). Omori, Shigetoshi; Sakakibara, Akira (Fac. Agric., Hokkaido Univ., Sapporo, Japan). Mokuzai Gakkaishi, 19(1), 41-4 (Japanese) 1973. CODEN: MKZGA7. ISSN: 0021-4795.
AB The title wood meal was extd. with 1:2 EtOH-benzene, concd., and extd. with petroleum ether to give (-)-.alpha.-conidendrin (I) [518-55-8] and (-)-**hydroxymatairesinol** (II).

L10 ANSWER 49 OF 53 CAPLUS COPYRIGHT 2003 ACS
1971:506237 Document No. 75:106237 Phenolic extractives in Norway spruce and their effects on Fomes annosus. Shain, Louis; Hillis, W. E. (Div. Forest Prod., CSIRO, South Melbourne, Australia). Phytopathology, 61(7), 841-5 (English) 1971. CODEN: PHYTAJ. ISSN: 0031-949X.
GI For diagram(s), see printed CA Issue.
AB **Hydroxymatairesinol** (I), matairesinol, liovil, and conidendrin were identified in healthy heartwood tissue of Norway spruce (Picea abies) as well as in the reaction zone sepg. healthy sapwood from wood decayed by F. annosus. The reaction zone contained considerably more I than was found in heartwood. Healthy sapwood and wood in advanced stages of decay contained negligible quantities of **lignans**. I was significantly more inhibitory to F. annosus than was matariresinol or conidendrin in vitro. I in assocn. with the alkalinity in the reaction zone may contribute to the resistance of the sapwood to F. annosus in vivo.

L10 ANSWER 50 OF 53 CAPLUS COPYRIGHT 2003 ACS
1970:511114 Document No. 73:111114 Cellular distribution of **lignans** in Tsuga heterophylla wood. Krahmer, R. L.; Hemingway, R. W.; Hillis, W. E. (Forest Prod. Lab., C.S.I.R.O., South Melbourne, Australia). Wood Science and Technology, 4(2), 122-39 (English) 1970. CODEN: WOSTBE. ISSN: 0043-7719.
AB Western hemlock heartwood contained tracheids with large amts. of cellular inclusions and deposits contg. the **lignans** matairesinol, **hydroxymatairesinol**, and conidendrin. The deposits occurred in 3 different forms and various chem. compns. Rays contained deposits phys. similar to those in adjacent tracheids, but did not contain **lignans**, although **lignans** were present in the tracheids. **Lignans** formed surface films on tracheid walls and encrusted the bordered pits. The amt. of **lignans** was not related to wet wood zones. The **lignan** biosynthesis probably occurred in the heartwood periphery in the vicinity of the half-bordered pits.

L10 ANSWER 51 OF 53 CAPLUS COPYRIGHT 2003 ACS
1963:421478 Document No. 59:21478 Original Reference No. 59:3815h,3816a-e Pinoresinolide and other intermediates of lignin formation. Freudenberg, Karl; Geiger, Hans (Univ. Heidelberg, Germany). Ber., 96, 1265-70 (Unavailable) 1963.
GI For diagram(s), see printed CA Issue.
AB Ferulic acid (I) was found among the dehydrogenation products of coniferyl alc. (II). The dehydrogenation product of I condenses with dehydrogenated II to give 4-oxo-2,6-bis(4-hydroxy-3-methoxyphenyl)-3,7-dioxabicyclo[3.3.0]octane (pinoresinolide) (III), which corresponds to pinoresinol (IV) and is a **lignan**. A 2nd **lignan** is the isomeric compd. V (substance 13) which is related to

hydroxymatairesinol and thus to conidendrin. These **lignans**, III and V, are responsible for the infrared lactone band in the spectra of conifer lignin and artificial lignin. The oligomer mixt. obtained by the method described previously (CA 58, 2581e) extd. with EtOAc, the concd. ext. subjected to a countercurrent distribution with 1:4:5 HCONMe2-H2O-Et2O, the fractions moving faster than dehydro-diconiferyl alc. (VI) and contg. IV combined and evapd., and the sirupy residue (5 g.) in 10 cc. Me2CO chromatographed on Perlon powder gave the following substances in the order given: II dihydro deriv. (VII), II, IV with coniferyl aldehyde, and VI, III, V, vanillic acid (VIII) (substance 10), and mixed cis- and trans-I (substance 9). The crude I recrystd. from H2O gave trans-II, m. 170-1.degree.. The residue from the fractions contg. the VIII chromatographed on thick paper sheets gave pure VIII, m. 210-11.degree.. The Me2CO fraction contg. the III evapd. slowly during several days gave platelets of III, m. 127-8.degree.. I (1.94 g.), 0.42 g. NaHCO3, 1 l. H2O, and 200 cc. citrate buffer (pH 5.5) treated with 5 mg. peroxidase and then during 5 days dropwise simultaneously with 1 l. 0.02N H2O2 and 1.8 g. II in 10 cc. dioxane and 990 cc. H2O while adding an addnl. 1 mg. peroxidase/day, satd. with NaCl, and extd. with EtOAc, and the residue from the ext. chromatographed on Perlon yielded 200-20 mg. III. III (50 mg.) in 0.5 cc. Ac2O and 0.4 cc. C5H5N heated 15 hrs. at 40.degree., dild. with iced H2O to 10 cc., and kept several hrs. at 0.degree. yielded the diacetate of III, cryst. powder, m. 125.degree. (1:10 C6H6-CCl4). III (200 mg.) in 10 cc. MeOH treated 24 hrs. with 0.840 g. CH2N2 in 40 cc. Et2O and evapd. gave the di-Me ether of III, platelets, m. 126-7.degree. (aq. Me2CO). III (30 mg.) and 30 mg. 2,4-(O2N)2C6H3F in 0.8 cc. HCONMe2 stirred 5 hrs. with 0.2 cc. 9% aq. NaHCO3, treated with an addnl. 0.5 cc. NaHCO3, dild. after 3 hrs. with 5 cc. H2O, and filtered yielded the bis(2,4-dinitrophenyl) ester of III, pale yellow, amorphous powder, m. 109-11.degree. (repptd. from Me2CO with MeOH). The light yellow-brown sirupy V dissolved in boiling CH2Cl2, filtered, and concd. to turbidity deposited 70-80 mg. V, colorless powder, which was converted in the usual manner to the bis(2,4-dinitrophenyl) ether. The Rf values were detd. for the following compds.: II 0.29, III 0.33, V 0.41, IV 0.47, VI A1 0.53, II 0.55, VI A2 0.57, VII 0.73, trans-I 0.85, VIII 0.89, cis-I 0.9.

L10 ANSWER 52 OF 53 CAPLUS COPYRIGHT 2003 ACS

1962:60384 Document No. 56:60384 Original Reference No. 56:11478a-c System and nomenclature of **lignans**. Freudenber, K.; Weinge, K. (Univ. Heidelberg, Germany). Tetrahedron, 15, 115-28 (Unavailable) 1961.

AB -A system of notation for **lignans** and isolignans is proposed and renaming of isolignans as cyclolignans suggested. The basic hydrocarbons are designated as **lignan** and cyclolignan and the notation is based on the oxygen equivs. in the benzene rings and side chains. The classification is according to the no. of O atoms in the left and in the right benzene ring of the proposed structural for mulation and within the classes the order follows the oxidn. stage outside the benzene rings, i.e., **hydroxymatairesinol** has 1 equiv. at C-7 and C-9 and 3 equivs. at C-9', altogether five (V) and is classified as 2:2:V (-)-**hydroxymatairesinol**. A list of 51 available natural **lignans** is tabulated, giving in the title the no., classification and usual name, and below (a) the systematic designation, (b) the proposed new designation including configuration, and (c) the abbreviated designation with systematic indication of configuration; e.g., (7) 2:2:II (-)-galbelgin, (a) 3,4-dimethyl-2,5-bis[3,4dimethoxyphenyl]tetrahydrofuran , (b) 3,4,3',4'-tetrameth-oxy-7,7'-epoxy-.alpha.7..beta.8, .beta.7'..alpha.8'-**lignan**, (c) (7S.8S.7'S.8'S)-7.7'-epoxyguaialignan dimethyl ether.The structural formulas follow the proposed conventions for lay-out, numbering and indication of configuration.

L10 ANSWER 53 OF 53 CAPLUS COPYRIGHT 2003 ACS

1958:88001 Document No. 52:88001 Original Reference No. 52:15494c-i,15495a-i,15496a-c The **lignans** of fir wood. Freudenberg, Karl; Knof, Leo (Univ. Heidelberg, Germany). Chem. Ber., 90, 2957-69 (Unavailable) 1957.

AB A 20-30 years old fir freed of its bark and dried, resin-free pieces reduced to saw dust, 4-kg. portions air-dried saw dust each in three 16-1. percolators extd. with 85% aq. Me2CO, the 1st 20 l. percolate from the 1st percolator passed through the 2nd and 3rd percolator during 10 days, the percolate from a total of 40 kg. wood evapd. in vacuo, the tacky residue (637 g.) added to 400 cc. anhyd. Me2CO, the resulting 2 phases centrifuged from a small amt. of solid, the 2-phase supernatant evapd. in vacuo, a 100-g. portions of the solid residue dissolved in 100 cc. 4:1 HCONH2-H2O, the soln. washed with three 60-cc. portions Et2O, and the Et2O washing and the aq. soln. subjected to a countercurrent distribution with 1:3 HCONH2-H2O (satd. with Et2O) yielded the following fractions (designation of fraction, tube no., color of coupling product with diazotized sulfanilic acid in 2% aq. Na2CO3, % of charge, and main components given): A, up to 238, almost none, 29.3, phenol-free material; B, 239-660, red, 9.5, red-coupling **lignans**; C, 661-1278, yellow, 16.2, **hydroxymatairesinols**; D, 1279-2100, yellow, 3.6, liovil (I); E, 2101-2380 and 120-200, yellow, 2.5, yellow-coupling substances; F, 70-119, yellow, 1.7, yellow-coupling substances; G, 35-69, yellow, 3.3, yellow-coupling substances; H, 1-34, yellow, 9.6, dissolved lignin portion; I, 1-34, yellow, 20.3, undissolved lignin portion. The phenol free resin fraction A (60 g.) distd. at 0.4 mm. to 300.degree. gave 35 g. distillate which redistd. yielded 14 g. distillate, b0.01 to 180.degree., and 15 g. distillate, b0.01 180-98.degree.. The first distillate fraction hydrogenated gave 4.5 g. stearic acid. Fraction B (37 g.) gave after removal of the Et2O 5 g. cryst. (-)-.alpha.-conidendrin (II), m. 238.degree. with resolidification and rem. 256.degree. (HCO2H and EtOH), [.alpha.]25D -71.4.degree. (c 4, tetrahydrofuran), -54.5.degree. (Me2CO); II freshly recrystd. from HCO2H showed sometimes a m.p. of 242-3.degree. with resolidiflcation and rem. 262-3.degree.. The mother liquor from the II evapd., the residue dissolved in tetrahydrofuran, the soln. evapd., the residue (31 g.) redissolved in 80 cc. HCONH2, and the soln. subjected to a countercurrent distribution with 1:1 HCONH2-H2O (satd. with Et2O) yielded the following fractions (same data given): B-1, to 347, almost none, 6, phenol-free materials; B-2, 348-447, lemon-yellow with blue fluorescence, 7, coniferylaldehyde (III) with little 3,4-divanillyltetrahydrofuran (IV) and vanillin (V); B-3, 448-687, red, 21, pinoresinol (VI) and matairesinol (VII); B-4, 688-1005, gray-red, 20, II with a little VII; B-5, 1000-1349, red-violet, 14, oxomatairesinol (VIII) and II; B-6, 1350-1728, red, 9, lariciresinol (IX) with a little II; B-7, 1729-1915 and 160-200, red, 4, II with a little **hydroxymatairesinols**; B-8, 100-159, yellow, 7, **hydroxymatairesinols**; B-9, 1-99, yellow, 2, -. Fraction B-2 in EtOH treated with KOAc in EtOH, the adduct treated with H2O contg. a small amt. of hydroquinone and filtered, and the residue dried and recrystd. from C6H6 contg. a trace of hydroquinone gave III; 2,4-dinitrophenylhydrazone, m. 266-9.degree.. The filtrate from the adduct evapd., the residue treated with CH2Cl2 and H2O, the org. layer evapd., and the residue dissolved in EtOH and treated with 3 g. 2,4-(O2N)2C6H3NHNH2 in 100 cc. EtOH and 2 cc. concd. HCl gave the 2,4-dinitrophenylhydrazone of V, m. 266-7.degree.. The presence of IV in fraction B-2 was demonstrated by the paper chromatogram. Fraction B-3 (3.5 g.) ground with 6 cc. satd. alc. KOAc, allowed to stand 6 hrs., and filtered, and the residue washed with alc. KOAc and decompd. with CH2Cl2 and H2O yielded 1.4 g. (crude) (+)-VI, m. 119-20.degree. (EtOH), contg. 13% (.+-.)-VI, which recrystd. further gave 94%-pure (+)-VI, [.alpha.]21D 84.4.degree. (c 5, Me2CO). Fraction B-3 (4 g.) combined with 2 g. residue from the isolation of the VI and dissolved in 50 cc. CHCl3, and the soln. subjected to a 495-transfer countercurrent distribution yielded in the tubes 142-192 1.26 g. (crude) (-)-VII, m. 116-18.degree. (30% aq. AcOH),

[.alpha.]25D -45.0.degree. (c 4.2, Me2CO); di-Me ether, m. 129-30.degree., [.alpha.]25D -31.8.degree. (c 1.7, CHCl3). Fraction B-4 digested with a little AmOH and filtered gave II. Fraction B-5 (4 g.) in 25 cc. CHCl3 subjected to a 375-transfer countercurrent distribution with 3:2.5:6 HCONH2-H2OCHCl3 yielded in tubes 80-118 2 g. (+)-VIII, m. 70-2.degree., [.alpha.]25D 42.6.degree. (c 4.0, tetrahydrofuran) (diacetate, needles, m. 122-3.degree. (EtOH)], and in tubes 20-42 0.8 g. II. VIII in EtOAc hydrogenated in the presence of PdCl2 yielded VII, m. 116-17.degree., [.alpha.]25D -45.1.degree. (c Me2CO). VIII in EtOAc hydrogenated 2 days over 5% Pd-kieselguhr gave in addn. to VII and VIII also (-)-**hydroxymatairesinol** (X), and (-)-allohydroxymatairesinol (XI); the crude product treated with alc. KOAc gave the X-KOAc adduct, m. 120-2.degree.. Fraction B-6 crystd. partially to deposit IX. The combined fractions C and B-8 (10 g.)in 15 cc. HCONH2 and 3 cc. H2O subjected to a 2630-transfer countercurrent distribution with 1:3.5:5 HCONH2-H2O-CHCl3 gave 2.7 g.-amorphous X, [.alpha.]22D -11.0.degree. (c 4.0, tetrahydrofuran), -6.3.degree. (c 4, EtOH), and 4.0 g. XI, [.alpha.]25D -9.8.degree. (c 4.0, tetrahydrofuran), 4.9.degree. (c 4, EtOH). A mixt. (10 g.) of X and XI kept 1 day at 20.degree. with 10 cc. satd. alc. KOAc and filtered, and the residue washed with a little PrOH yielded 6.5 g. X-KOAc adduct, m. 126-7.degree. (BuOH). X gave also with PrOH satd. with EtCO2K a cryst. adduct. X-KOAc adduct (6 g.) dissolved in a few cc. 2:3 Me2CO-H2O, shaken with 70 cc. H2O and 75 cc. CH2Cl2, the aq. layer extd. with CH2Cl2, and the combined CH2Cl2 solns. evapd. while protected from light gave 4.4 g. colorless residue; X-XI mixt. heated with alc. KOAc yielded with the disappearance of the X-XI apparently higher mol. wt. orange-yellow coupling material. X (1 g.) dissolved in 60.degree. in 1 g. NaOH in 1 cc. H2O, cooled, neutralized with 50% AcOH, cooled with ice, and filtered, the residue washed with dil. aq. NaOAc, dissolved in 10 cc. MeOH, and the soln. dild. with 15 cc. C6H6 gave 0.3 g. Na (-)-hydroxymatairesinolate, prisms, which acidified with moderately dil. AcOH gave oily crystals. X with 2,4-(O2N)2C6H3F gave a yellow amorphous powder which subjected to countercurrent distribution with 5:3.5:1.5, CH2Cl2-MeOH-H2O, then with 3:2:1:0.6, and finally with 5:4.5:1.5:1 HCONMe2-C6H6-cyclohexane-H2O yielded the 2,4-dinitrophenyl ether deriv. of X, amorphous solid; acetate, amorphous solid. X with CH2N2 gave the di-Me ether, m. 96-7.degree. (AmOH), [.alpha.]25D 59.8.degree. (c 2.0, tetrahydrofuran). X (0.5 g.) in EtOAc hydrogenated over 0.2 g. Pd during 16 hrs., filtered, and evapd., and the residue recrystd. from 3:7 glacial AcOH-H2O yielded 71% (-)-VII. XI gave similarly 50% (-)-VII. II converted to the di-Me ether and then treated with Pb(OAc)2 gave a phenylnaphthalene deriv., m. 216-17.degree. with resolidification and rem. 225-7.degree.. X (0.20 g.) in 5 cc. of a soln. of 1 cc. concd. H2SO4 in 20 cc. tetrahydrofuran showed the following [.alpha.]25D values at the times in min. given in parentheses: -6.1.degree. (10), 1.4.degree. (35), 11.7.degree. (105), 19.0.degree. (260), 19.4.degree. (290), 3.1.degree. (1185), -1.7.degree. (1415), -21.6.degree. (2520), -42.4.degree. (4140), -56.8.degree. (5950), -58.0.degree. (6000). This change of rotation indicates a conversion of X to II. Fraction D (3.5 g.) digested with 8 cc. AmOH, refrigerated 18 hrs., and filtered gave 0.8 g. (-)-I, prisms, m. 173.5-4.5.degree. (aq. MeOH), [.alpha.]25D -32.8.degree. (c 4.0, MeOH); tetraacetate, m. 124-5.degree. (EtOH). The AmOH ext. from fraction D evapd., the residue dissolved warm in 375 cc. CHCl3 and 375 cc. H2O, and the mixt. subjected to a 185-transfer countercurrent distribution gave in tubes 90-125 an addnl. 0.36 g. (-)-I. (-)-I (0.25 g.) in EtOAc hydrogenated 2 days over 0.2 g. Pd black gave IV, prisms, m. 116-17.degree. (Me3COH), [.alpha.]25D -52.2.degree. (c 1.4, tetrahydrofuran). VI in EtOAc hydrogenated 1.5 hrs. over prehydrogenated PdCl2 and the mixt. chromatographed on paper showed the presence of VI, IX, and 2,3-divanillyl-1,4-butanediol, Rf 0.85 (HCONH2-Et2O), which coupled with a red-violet color; the mixt. dehydrated by the method of Haworth and Woodcock (C.A. 33, 68332) yielded 35% IV, m. 116-17.degree..

(+)-IX hydrogenated in EtOAc in the usual manner yielded during 40 min. 70% IV, [.alpha.]25D -51.8.degree. (c 4.0, tetrahydrofuran). IV showed the following Rf values with the listed solvents satd. with HCONH2: Et2O 0.67, CHCl3 0.91, CHCl:CCl2 0.67, PhCl 0.66, C6H6 0.61, CCl4 0.35, cyclohexane 0.02. IX showed under the same conditions the following Rf values: Et2O 0.14, CHCl3 0.38, PhCl 0.04, C6H6 0.03, CH2Cl2 0.34. IV showed the following Rf values with the listed solvents half-satd. with HCONH2: MECH-(OMe)2 0.68, MeCH(OEt)2 0.64. IX showed under the same conditions the following Rf values: MeCH(OMe)2 0.43, MeCH(OEt)2 0.18 ,CH2Cl2 0.41. The Rm values (cf. Brooks, et al., C.A. 51, 12113d) were detd. for the following compds.: dehydrodiisoeugenol -0.85, dehydrodiconiferyl alc. 0.91, X 1.00, VII 0.25, I 1.28, IV -0.25, VIII 0.63, II 0.42. From these values were calcd. the following Rf group increments: OH (.gamma.) 0.88, OH (.alpha.) 0.75, OH (.alpha.) 0.76, .alpha.-oxo group 0.38, ring closure with the loss of 2H 0.17. The red coupling amorphous trace amts. (accompanying II in fraction B) with Rf 0.54-0.55 might possibly be 2,5-diguaiacyl-3,4-dimethyltetrahydrofuran for which an Rf value of 0.54 is calcd.

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=> s l2 and neutrophils
L11           0 L2 AND NEUTROPHILS

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     (FILE 'HOME' ENTERED AT 13:39:04 ON 06 MAY 2003)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 13:39:17 ON
     06 MAY 2003
L1          120 S HYDROXYMATAIRESINOL
L2           53 S L1 AND MATAIRESINOL
L3           16 S L2 AND ENTEROLACTONE
L4            5 DUP REMOVE L3 (11 DUPLICATES REMOVED)
L5          105 S L1 AND LIGNAN
L6            0 S L5 AND PHAGOCYTES
L7            0 S L5 AND OXIDATIVE BURST
L8            0 S L5 AND NEUTROPHILS
L9            0 S L5 AND MYELOID
L10          53 DUP REMOVE L5 (52 DUPLICATES REMOVED)
L11           0 S L2 AND NEUTROPHILS

=> s l2 and oxidative burst
L12           0 L2 AND OXIDATIVE BURST

=> s l2 and lignan
L13          45 L2 AND LIGNAN

=> s l13 and lymphocyte
L14           0 L13 AND LYMPHOCYTE

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MISSING OPERATOR S L3
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nested terms that are not separated by a logical operator.

=> s l13 and ischemia reperfusion injury
L15           0 L13 AND ISCHEMIA REPERFUSION INJURY

=> s l13 and stroke
L16           0 L13 AND STROKE

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PROCESSING COMPLETED FOR L13
L17 29 DUP REMOVE L13 (16 DUPLICATES REMOVED)

=> d l17 1-29 cbib abs

L17 ANSWER 1 OF 29 MEDLINE DUPLICATE 1
2003073811 Document Number: 22472537. PubMed ID: 12583751. Synthesis of (-)-**matairesinol**, (-)-enterolactone, and (-)-enterodiol from the natural **lignan hydroxymatairesinol**. Eklund Patrik; Lindholm Anna; Mikkola J-P; Smeds Annika; Lehtila Reko; Sjoholm Rainer. (Department of Organic Chemistry, Abo Akademi University, Biskopsgatan 8, 20500-FIN, Abo, Finland.) ORGANIC LETTERS, (2003 Feb 20) 5 (4) 491-3. Journal code: 100890393. ISSN: 1523-7060. Pub. country: United States. Language: English.
AB We describe here a four-step semisynthetic method for the preparation of enantiomerically pure (-)-enterolactone starting from the readily available **lignan hydroxymatairesinol** from Norway spruce (Picea abies). **Hydroxymatairesinol** was first hydrogenated to **matairesinol**. **Matairesinol** was esterified to afford the matairesinyl 4,4'-bistriflate, which was deoxygenated by palladium-catalyzed reduction to 3,3'-dimethylenterolactone. Demethylation of 3,3'-dimethylenterolactone and reduction with LiAlH(4) yielded (-)-enterolactone and (-)-enterodiol, respectively.

L17 ANSWER 2 OF 29 MEDLINE DUPLICATE 2
2002484700 Document Number: 22231703. PubMed ID: 12270222. Structural determinants of plant **lignans** for the formation of enterolactone in vivo. Saarinen Niina M; Smeds Annika; Makela Sari I; Ammala Jenni; Hakala Kristo; Pihlava Juha-Matti; Ryhanen Eeva-Liisa; Sjoholm Rainer; Santti Risto. (Department of Anatomy, Institute of Biomedicine, University of Turku, FIN-20520, Turku, Finland.) J Chromatogr B Analyt Technol Biomed Life Sci, (2002 Sep 25) 777 (1-2) 311-9. Journal code: 101139554. ISSN: 1570-0232. Pub. country: United States. Language: English.
AB The quantity of mammalian **lignans** enterolactone (ENL) and enterodiol (END) and of plant **lignans** secoisolariciresinol (SECO) and 7-**hydroxymatairesinol** (HMR) excreted in a 24-h rat urine sample was measured after a single p.o. dose of an equivalent quantity of secoisolariciresinol diglycoside (SDG), secoisolariciresinol (SECO), **matairesinol** (MR), 7-**hydroxymatairesinol** (HMR) and ENL. Plant **lignans** (SECO and HMR) were partially absorbed as such. The aglycone form of SECO was more efficiently converted into mammalian **lignans** END and ENL than the glycosylated form, SDG. Of plant **lignans**, MR produced the highest quantities of ENL: the quantity was over twofold compared with HMR or SDG. The majority of the animals, which had been given SECO, excreted higher quantities of END than ENL into urine, but ENL was the main **lignan** metabolite after SDG. The highest quantities of ENL in urine were measured after the administration of ENL as such. The (-)SECO isolated from Araucaria angustifolia was converted into (-)ENL only. The administration of (-)SDG, which was shown to produce (+)SECO, resulted in excretion of (+)ENL only and (-)HMR was converted into (-)ENL only. This confirmed that the absolute configurations at C8 and C8' are not changed during the microbial metabolism. Whether the biological effects are enantiomer-specific, remains to be resolved.

L17 ANSWER 3 OF 29 MEDLINE DUPLICATE 3
2001423900 Document Number: 21347776. PubMed ID: 11453749. In vitro metabolism of plant **lignans**: new precursors of mammalian **lignans** enterolactone and enterodiol. Heinonen S; Nurmi T; Liukkonen K; Poutanen K; Wahala K; Deyama T; Nishibe S; Adlercreutz H. (Folkhalsan Research Center and Department of Clinical Chemistry, P.O. Box

60, FIN-00014 University of Helsinki, Finland.) JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY, (2001 Jul) 49 (7) 3178-86. Journal code: 0374755. ISSN: 0021-8561. Pub. country: United States. Language: English.

AB The metabolism of the plant **lignans matairesinol**, secoisolariciresinol, pinoresinol, syringaresinol, arctigenin, 7-**hydroxymatairesinol**, isolariciresinol, and lariciresinol by human fecal microflora was investigated to study their properties as mammalian **lignan** precursors. The quantitative analyses of **lignan** precursors and the mammalian **lignans** enterolactone and enterodiol were performed by HPLC with coulometric electrode array detector. The metabolic products, including mammalian **lignans**, were characterized as trimethylsilyl derivatives by gas chromatography-mass spectrometry. **Matairesinol**, secoisolariciresinol, lariciresinol, and pinoresinol were converted to mammalian **lignans** only. Several metabolites were isolated and tentatively identified as for syringaresinol and arctigenin in addition to the mammalian **lignans**. Metabolites of 7-**hydroxymatairesinol** were characterized as enterolactone and 7-hydroxyenterolactone by comparison with authentic reference compounds. A metabolic scheme describing the conversion of the most abundant new mammalian **lignan** precursors, pinoresinol and lariciresinol, is presented.

L17 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2003 ACS

2002:543197 Document No. 137:216291 Uptake and metabolism of **hydroxymatairesinol** in relation to its anticarcinogenicity in DMBA-induced rat mammary carcinoma model. Saarinen, Niina M.; Huovinen, Riikka; Waerri, Anni; Maekelae, Sari I.; Valentin-Blasini, Liza; Needham, Larry; Eckerman, Christer; Collan, Yrjoe U.; Santti, Risto (Department of Anatomy, Institute of Biomedicine, University of Turku, Turku, FIN-20520, Finland). Nutrition and Cancer, 41(1&2), 82-90 (English) 2001. CODEN: NUCADQ. ISSN: 0163-5581. Publisher: Lawrence Erlbaum Associates, Inc..

AB The chemopreventive effects of **hydroxymatairesinol** (HMR), a **lignan** extd. from Norway spruce (Picea abies), on the development of mammary carcinoma induced by 7,12-dimethylbenz[a]anthracene (DMBA) was studied in rats. HMR administered via diet in an av. daily dose of 4.7 mg/kg body wt starting before DMBA induction reduced tumor vol. and tumor growth, but no significant redn. in tumor multiplicity (no. of tumors/rat) was obsd. The predominant histol. type in the control group was type B (well-differentiated adenocarcinoma, 78%). The proportion of type B tumors decreased to 35% in the HMR group, while the type A (poorly differentiated) and type C (atrophic) tumor proportions increased. Anticarcinogenic effects of dietary HMR (4.7 mg/kg) were also evident when the administration started after DMBA induction and was seen as growth inhibition of established tumors. Dietary HMR supplementation significantly increased serum and urinary enterolactone and HMR concns. but had no significant effect on the uterine wt., suggesting that HMR or its major metabolite enterolactone did not have an anti-estrogenic effect. Further studies are warranted to further clarify and verify HMR action and the assocd. mechanisms in mammary tumorigenesis.

L17 ANSWER 5 OF 29 MEDLINE DUPLICATE 4

2001129080 Document Number: 21016670. PubMed ID: 11130663. Dirigent-mediated podophyllotoxin biosynthesis in Linum flavum and Podophyllum peltatum. Xia Z Q; Costa M A; Proctor J; Davin L B; Lewis N G. (Institute of Biological Chemistry, Washington State University, Pullman 99164-6340, USA.) PHYTOCHEMISTRY, (2000 Nov) 55 (6) 537-49. Journal code: 0151434. ISSN: 0031-9422. Pub. country: United States. Language: English.

AB Given the importance of the antitumor/antiviral **lignans**, podophyllotoxin and 5-methoxypodophyllotoxin, as biotechnological targets, their biosynthetic pathways were investigated in Podophyllum peltatum and

Linum flavum. Entry into their pathways was established to occur via dirigent mediated coupling of E-coniferyl alcohol to afford (+)-pinoresinol; the encoding gene was cloned and the recombinant protein subsequently obtained. Radiolabeled substrate studies using partially purified enzyme preparations next revealed (+)-pinoresinol was enantiospecifically converted sequentially into (+)-lariciresinol and (-)-secoisolariciresinol via the action of an NADPH-dependent bifunctional pinoresinol/lariciresinol reductase. The resulting (-)-secoisolariciresinol was enantiospecifically dehydrogenated into (-)-**matairesinol**, as evidenced through the conversion of both radio- and stable isotopically labeled secoisolariciresinol into **matairesinol**, this being catalyzed by the NAD-dependent secoisolariciresinol dehydrogenase. (-)-**Matairesinol** was further hydroxylated to afford 7'-**hydroxymatairesinol**, this being efficiently metabolized into 5-methoxypodophyllotoxin. Thus much of the overall biosynthetic pathway to podophyllotoxin has been established, that is, from the dirigent mediated coupling of E-coniferyl alcohol to the subsequent conversions leading to 7'-**hydroxymatairesinol**.

L17 ANSWER 6 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 5
2000415530 EMBASE Chemopreventive activity of crude hydroxsymatairesinol (HMR) extract in Apc(Min) mice. Oikarinen S.I.; Pajari A.-M.; Mutanen M.. M. Mutanen, Dept. of Applied Chem./Microbiol., University of Helsinki, P.O. Box 27, FIN-00014, Helsinki, Finland. marja.mutanen@helsinki.fi. Cancer Letters 161/2 (253-258) 20 Dec 2000.
Refs: 18.
ISSN: 0304-3835. CODEN: CALEDQ.
Publisher Ident.: S 0304-3835(00)00543-7. Pub. Country: Ireland. Language: English. Summary Language: English.

AB We studied the effects of a **lignan, hydroxymatairesinol** (HMR), and rye bran on intestinal tumor development in adenomatous polyposis colimultiple intestinal neoplasia (Apc)(Min) mice. HMR showed a strong chemopreventive effect in this animal model. The mean number of adenomas in the small intestine was significantly lower (26.6 .+-. 11.0, P < 0.05) in mice fed the inulin and HMR when compared with the inulin and inulin/rye bran fed mice (39.6 .+-. 8.9 and 36.0 .+-. 7.4, respectively). HMR resulted in normalization of .beta.-catenin levels in adenoma tissue, indicating that HMR mediates its chemopreventive effect through the Apc-.beta.-catenin pathway. In the cytosolic fraction, .beta.-catenin level in adenoma tissue was significantly elevated (P = 0.008-0.013) in all the diet groups as compared with that of the surrounding mucosa. In the nuclear fraction, .beta.-catenin in the inulin (3.15 .+-. 2.9 relative units) and inulin/rye (5.17 .+-. 6.94 relative units) groups was also significantly higher (P = 0.003-0.009) in the adenoma tissue when compared with the surrounding mucosa (0.5 .+-. 0.5 and 0.35 .+-. 0.39 relative units). However, HMR was able to restore nuclear .beta.-catenin level of the adenoma tissue (0.41 .+-. 0.25 relative units) to the level found in the surrounding mucosa (0.36 .+-. 0.28 relative units). (C) 2000 Published Elsevier Science Ireland Ltd.

L17 ANSWER 7 OF 29 MEDLINE DUPLICATE 6
2001103469 Document Number: 20348508. PubMed ID: 10890032.
Hydroxymatairesinol, a novel enterolactone precursor with antitumor properties from coniferous tree (Picea abies). Saarinen N M; Warri A; Makela S I; Eckerman C; Reunanen M; Ahotupa M; Salmi S M; Franke A A; Kangas L; Santti R. (Department of Anatomy, University of Turku, Finland.) NUTRITION AND CANCER, (2000) 36 (2) 207-16. Journal code: 7905040. ISSN: 0163-5581. Pub. country: United States. Language: English.

AB The potential for the extraction of the plant **lignan** **hydroxymatairesinol** (HMR) in large scale from Norway spruce (Picea abies) has given us the opportunity to study the metabolism and biological actions of HMR in animals. HMR, the most abundant single component of

spruce **lignans**, was metabolized to enterolactone (ENL) as the major metabolite in rats after oral administration. The amounts of urinary ENL increased with the dose of HMR (from 3 to 50 mg/kg), and only minor amounts of unmetabolized HMR isomers and other **lignans** were found in urine. HMR (15 mg/kg body wt po) given for 51 days decreased the number of growing tumors and increased the proportion of regressing and stabilized tumors in the rat dimethylbenz[a]anthracene-induced mammary tumor model. HMR (50 mg/kg body wt) did not exert estrogenic or antiestrogenic activity in the uterine growth test in immature rats. HMR also showed no antiandrogenic responses in the growth of accessory sex glands in adult male rats. Neither ENL nor enterodiol showed estrogenic or antiestrogenic activity via a classical alpha- or beta-type estrogen receptor-mediated pathway in vitro at < 1.0 microM. HMR was an effective antioxidant in vitro.

L17 ANSWER 8 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
2000340272 EMBASE Chemopreventive activity of hydroksymatairesinol in adenomatous polyposis colimultiple intestinal neoplasia (Apc)(Min) mice. Oikannen S.I.; Pajari A.-M.; Mutanen M.. M. Mutanen, Dept. of Appl. Chem. and Microbiol., University of Helsinki, P.O. Box 27, FIN-00014 Helsinki, Finland. maria.mutanenc@helsinki.fi. Cancer Letters 159/2 (183-187) 31 Oct 2000.
Refs: 15.
ISSN: 0304-3835. CODEN: CALEDQ.
Publisher Ident.: S 0304-3835(00)00543-7. Pub. Country: Ireland. Language: English. Summary Language: English.
AB We studied the effects of a **lignan, hydroxymatairesinol** (HMR), and rye bran on intestinal tumor development in adenomatous polyposis colimultiple intestinal neoplasia (Apc)(Min) mice. HMR showed a strong chemopreventive effect in this animal model. The mean number of adenomas in the small intestine was significantly lower (26.6 .+-. 11.0, P < 0.05) in mice fed the TNS tumor promoter insulin and HMR when compared with the insulin and insulin/rye bran fed mice (39.6 .+-. 8.9 and 36.0 .+-. 7.4, respectively). HMR resulted in normalization of .beta.-catenin levels in adenoma tissue, indicating that HMR mediates its chemopreventive effect through the Apc-.beta.-catenin pathway. In the cytosolic fraction, .beta.-catenin level in adenoma tissue was significantly elevated (P = 0.008-0.013) in all the diet groups as compared with that of the surrounding mucosa. In the nuclear fraction, .beta.-catenin in the insulin (3.15 .+-. 2.9 relative units) and insulin/rye (5.17 .+-. 6.94 relative units) groups was also significantly higher (P = 0.003-0.009) in the adenoma tissue when compared with the surrounding mucosa (0.5 .+-. 0.5 and 0.35 .+-. 0.39 relative units). However, HMR was able to restore nuclear .beta.-catenin level of the adenoma tissue (0.41 .+-. 0.25 relative units) to the level found in the surrounding mucosa (0.36 .+-. 0.28 relative units). (C) 2000 Published by Elsevier Science Ireland Ltd.

L17 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2003 ACS
1999:693513 Document No. 132:33212 **Lignans**, flavonoids and phenolic derivatives from Taxus mairei. Yang, Shung-Jim; Fang, Jim-Min; Cheng, Yu-Shia (Department of Chemistry, National Taiwan University, Taipei, 106, Taiwan). Journal of the Chinese Chemical Society (Taipei), 46(5), 811-818 (English) 1999. CODEN: JCCTAC. ISSN: 0009-4536. Publisher: Chinese Chemical Society.
AB From the twigs of Taxus mairei, 35 **lignans**, 2 sesquilignans, 4 flavonoids, 3 bisflavonoids, 13 phenolic derivs., 2 sesquiterpenes, 3 bisnorsesquiterpenes, 3 long-chain carboxylic acids and 4 steroids were isolated. The new **lignans** and phenolic glucosides include 7'-hydroxynortrachelogenin, 7-**hydroxymatairesinol**, 3'-O-demethylepipinoresinol, taxiresinol 9-acetate, 3'-O-demethyltanegool, 8'-epitanegool, 3,3'-dimethoxy-4,4',9-trihydroxy-7,9'-epoxylignan-7'-one, 3-O-demethyldihydrodehydrodiconiferyl alc., taxumaiglucoside A

heptaacetate, taxumaiglucoside B heptaacetate, and taxumaiglucoside C heptaacetate. Their structures were detd. by spectral methods.

L17 ANSWER 10 OF 29 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 7
94:740582 The Genuine Article (R) Number: PR974. THE EXTRACTIVES OF AOMORI TODOMATSU (ABIES-MARIESII MASTERS) - ISOLATIONS OF **LIGNANS** FROM THE HEARTWOOD. OMORI S (Reprint); OZAWA S; TANEDA K. SUNY SYRACUSE, COLL ENVIRONM SCI & FORESTRY, SYRACUSE, NY, 13210 (Reprint); IWATE UNIV, FAC AGR, MORIOKA, IWATE 020, JAPAN. MOKUZAI GAKKAISHI (1994) Vol. 40, No. 10, pp. 1107-1118. ISSN: 0021-4795. Pub. country: USA; JAPAN. Language: Japanese.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB This study examined the extractive components of Abies mariesii Masters (Aomori todomatsu). This hardy softwood species is grown primarily in the coldest region of the main island of Japan.

The ether and hexane soluble extractives from the heartwood of A. mariesii were determined. Ten compounds were identified from ether soluble fractions: alpha-conidendrin (I), **matairesinol** (II), ketomatairesinol (III), **hydroxymatairesinol** (IV), 1,2,3,4-tetrahydro-7-hydroxy-r-1-(4'-hydroxy-3'-methoxyphenyl)-t-2-hydroxymethyl-6-methoxy-c-3-naphthalenecarbaldehyde gamma-lactol (todolactol-B, V), t-4-(4'-hydroxy-3'-methoxybenzoyl)-r-2-(4''-hydroxy-3''-methoxyphenyl)-t-3-hydroxymethyl-tetrahydrofuran (VI), 2-hydroxy-t-4-[hydroxy(4'-hydroxy-3'-methoxyphenyl)methyl]-r-3-(4''-hydroxy-3''-methoxybenzyl)-tetrahydrofuran (todolactol-A, VII), t-4-(p-coumaroyloxy) (4'-hydroxy-3'-methoxyphenyl)methyl-2-hydroxy-r-3-(4''-hydroxy-3''-methoxybenzyl)-tetrahydrofuran (todolactol-A alpha'-p-coumarate, VIII),vanillic acid (IX),and t-4-[hydroxy (4'-hydroxy-3'-methoxyphenyl)methyl]-r-2-(4''-hydroxy-3''-methoxyphenyl)-t-3-hydroxymethyl-tetrahydrofuran (X), and beta-sitosterol (XI) was isolated and identified from the hexane soluble fraction. In this study the major features were a relatively large yield of **matairesinol** (II), comparable to that of compounds alpha-conidendrin (I) and **hydroxymatairesinol** (IV), and the presence of the lactol-type phenolic **lignans** such as Compounds (V), (VII), and (VIII).

L17 ANSWER 11 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
94211290 EMBASE Document No.: 1994211290. Taxoids from the roots of Taxus x medica cv. Hicksii. Appendino G.; Cravotto G.; Enriu R.; Gariboldi P.; Barboni L.; Torregiani E.; et al.. Dipt. Scienza/Tecnologia del Farmaco, via Giuria 9,10125 Torino, Italy. Journal of Natural Products 57/5 (607-613) 1994.
ISSN: 0163-3864. CODEN: JNPRDF. Pub. Country: United States. Language: English. Summary Language: English.
AB The roots of Taxus x media cv. Hicksii gave two new pseudoalkaloidal taxoids, identified as N-debenzoyl-N-butanoyl taxol [1] and 7.beta.-acetoxy-9- acetylspicataxine [2a]. A new baccatin IV derivative [7a] and the **lignans hydroxymatairesinol** [8] and (-)-epinortrachelogenin [9] were also isolated. The epoxidation of .DELTA.(4(20),11) taxadienes was investigated, disclosing an unusual reactivity of the bridgehead double-bond towards peracids. Regiochemically and stereochemically unnatural epoxides of taxoids were obtained. Nmr data for these compounds were compared with literature values on the natural epoxides. No significant correlation between the configuration of the 4(20)-oxirane ring and the chemical shift of H-5 was found.

L17 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2003 ACS
1990:79734 Document No. 112:79734 The wood extractives in alkaline peroxide bleaching of groundwood from Norway spruce. Ekman, Rainer; Holmbom, Bjarne (Lab. For. Prod. Chem., Abo Akad., Abo, SF-20500, Finland). Nordic Pulp & Paper Research Journal, 4(3), 188-91 (English) 1989. CODEN: NPPJEG. ISSN: 0283-2631.

AB The changes in extractive compn. of groundwood pulp from Norway spruce upon alk. H2O2 bleaching in a paper mill were investigated by gas chromatog. Only slight hydrolysis of esterified fatty acids occurred in bleaching and no significant alteration of the compn. of the fatty acids was obsd. No changes were found in the amt. and compn. of free and esterified sterols. However, considerable oxidn. of abietadienoic resin acids occurred whereas the pimaric-type resin acids and dehydroabietic acid were practically unaffected by bleaching. Among the polar extractives, the spruce **lignans** exhibited a drastic decrease including alkali-induced transformation of **hydroxymatairesinol** to conidendric acid. The spruce bark derived stilbenes were almost completely oxidized in bleaching. Alk. H2O2 bleaching produced a series of aliph. C2-C4 hydroxy and dicarboxylic acids. Glycolic, oxalic, 2-deoxytetronic and malic acids were the major components of this group.

L17 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2003 ACS

1989:121412 Document No. 110:121412 Pharmaceuticals containing leucoanthocyans for the treatment of alcoholism. Brekhman, I. I.; Bulanov, A. E.; Polozhentseva, M. I.; Mudzhiri, L. A.; Alkhazashvili, G. G.; Kalatozishvili, E. I.; Dardymov, I. V.; Bezdetko, G. N.; Khasina, E. I. (Institute of Biology of the Sea, Vladivostok, USSR; Scientific-Research Institute of Horticulture, Viticulture, and Wine Making). Ger. Offen. DE 3641495 A1 19880609, 21 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1986-3641495 19861204.

AB A pharmaceutical for the treatment of pathol. alc. addiction contains leucoanthocyans 219-270, catechins 153-187, flavonols 81-99, lignin 68-83, reducing saccharides 216-264, pectin 18-22, free amino acids 27-33, org. acids 36-44, sterols 4.5-5.5, methylsterols 1.35-1.65, dimethylsterols 1.98-2.42, **lignans** 13.5-16.5, **lignan** glycosides 9-11, phenolcarboxylic acids 13.5-16.5, phenolaldehydes 4.5-5.5, and alkyl ferulates 4.5-5.5 mg/g. Alc. rats received drinking water contg. 15% EtOH and 1 mL/50 mL of the above mixt. for 13 wk and were then kept abstinent for 10 days; in the abstinent animals the deprivation occurred without alc. withdrawal symptoms. Animals receiving the above mixt. and free to choose water or 15% EtOH-contg. water, decreased their EtOH consumption by 100% after the deprivation period, whereas alc. consumption increased in the control.

L17 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2003 ACS

1985:593134 Document No. 103:193134 A study of the constituents of the heartwood of Tsuga chinensis Pritz. var. formosana (Hay.). Fang, Jim Min; Wei, Kuo Min; Cheng, Yu Shia (Dep. Chem., Natl. Taiwan Univ., Taipei, Taiwan). Journal of the Chinese Chemical Society (Taipei, Taiwan), 32(1), 75-80 (English) 1985. CODEN: JCCTAC. ISSN: 0009-4536.

AB By means of spectroscopic anal., x-ray crystallog., and chem. correlation the heartwood of Taiwan hemlock was found to contain sterols, carboxylic acids, 13-epimanool, o-methoxyphenolics, coniferaldehyde, benzofuranoid neolignan, .alpha.-conidendrin, tsugacetal, isolariciresinol, secoisolariciresinol, **matairesinol**, **hydroxymatairesinol** and oxomatairesinol. Among them (+)-tsugacetal is a novel **lignan** acetal having an .alpha.-conidendrin-related structure with the acetal methoxy group at the .beta.-position.

L17 ANSWER 15 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

1982:255084 Document No.: BA74:27564. **LIGNANS** FROM TAXUS-WALLICHIANA. MILLER R W; MCLAUGHLIN J L; POWELL R G; PLATTNER R D; WEISLEDER D; SMITH C R. NORTH REG. RES. CENT., AGRIC. RES. SERV., US DEP. AGRIC., PEORIA, ILL. 61604.. J NAT PROD (LLOYDIA), (1982) 45 (1), 78-82. CODEN: JNPRDF. ISSN: 0163-3864. Language: English.

AB Three **lignans** were isolated from the roots, stems and needles of T. wallichiana Zucc. Two of these were identified as epimers of conidendrin and **hydroxymatairesinol**. The structure of the 3rd, a

previously unknown **lignan** named isoliovil, was established by 1H and 13C NMR and mass spectrometry.

L17 ANSWER 16 OF 29 CAPLUS COPYRIGHT 2003 ACS
1982:102372 Document No. 96:102372 Spectrophotometric determination of **lignans** in oakwood and brandy spirits. Kuridze, M. G.; Leont'eva, V. G.; Mudzhiri, L. A.; Semenov, A. A.; Lashkhi, A. D. (Nauchno-Issled. Inst. Sadovod., Vinograd. Vinodel., Tbilisi, USSR). Izvestiya Akademii Nauk Gruzinskoi SSR, Seriya Khimicheskaya, 7(3), 213-23 (Russian) 1981. CODEN: IGSKDH. ISSN: 0132-6074.
AB To det. lignin [9005-53-2] components, a sample (100 mL brandy or alc. ext. of oak wood) is concd., purified by column chromatog. on Chromaton N-AW, and resolved by TLC on silica gel. The individual components (secoisolariciresinol [29388-59-8], liovil [484-39-9], lariciresinol [27003-73-2], olivil [2955-23-9], pinoresinol [487-36-5], eudesmin [526-06-7], **matairesinol** [580-72-3], **hydroxymatairesinol** [20268-71-7], and isolariciresinol [548-29-8]) are sep. eluted with EtOH and the optical d. of each soln. is measured in a spectrophotometer (SF-26) at the appropriate wavelength in the UV region. The amt. of lignin component is computed from a calibration curve. The relative error of the method was .ltoreq.1.88%. The total lignin content in brandy increased upon storage from 41.4 mg/L (after 1 yr) to 140.9 mg/mL (after 20 yr).

L17 ANSWER 17 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
1982:189604 Document No.: BA73:49588. **LIGNANS** IN EASTERN HEMLOCK TSUGA-CANADENSIS. NAVAS S M; OMORI S. DEP. DE MADERAS, INST. TECNOL. DE COSTA RICA, APARTADO 159, CARTAGO, COSTA RICA A.C.. BULL IWATE UNIV FOR, (1981) 0 (12), 29-89. CODEN: IDNEAI. Language: English.
AB Comparisons of the chloroform-soluble extract components of eastern hemlock using standards from combined column chromatography, TLC and reverse phase high-pressure liquid chromatography [HPLC] techniques indicated the presence of the **lignans** pinoresinol, pinoresinol methyl ether, pinoresinol dimethyl ether, syringaresinol, conidendrin, **matairesinol**, oxomatairesinol, **hydroxymatairesinol**, liovil and isolariciresinol. Only conidendrin had been previously reported in eastern hemlock (Erdtman, 1944). .alpha.- and .beta.-Conidrendrol were not present in the heartwood chloroform-soluble extract. Although open column elution chromatography is a useful technique for the partial separation of natural mixtures of **lignans**, it is not adequate for the isolation of pure **lignans**. Silica gel or cellulose TLC was a good method for identification of **lignans**. The use of reverse phase HPLC in the analysis of **lignans** was not previously reported. Reverse phase HPLC is a sensitive and rapid method for the separation of **lignans**. Pinoresinol and conidendrin, e.g., were separable by reverse phase HPLC but were not readily separable by silica gel TLC. There were instances in which the technique could not distinguish between separate **lignans**. The following pairs of standards could not be separated: liovil and and **hydroxymatairesinol**, .alpha.-conidendrin and **matairesinol**, and pinoresinol and syringaresinol. The system was inadequate for the separation of liovil, **hydroxymatairesinol** and isolarioiresinol in natural mixtures. The reverse phase HPLC method is both rapid and relatively easy to use. Most of the peaks of the chromatograms were produced within 15 min of injection of the **lignan**-containing samples. The preparation of derivatives was unnecessary since pure compounds or mixtures can be injected into the chromatograph in their natural state.

L17 ANSWER 18 OF 29 CAPLUS COPYRIGHT 2003 ACS
1982:102368 Document No. 96:102368 Lignane in oak wood and cognac alcohols. Kuridze, M. G.; Mudzhiri, L. A.; Lashkhi, A. D.; Leont'eva, V. G.; Semenov, A. A. (Nauchno-Issled. Inst. Sadovod. Vinograd. Vinodel.,

Tbilisi, USSR). Vinodelie i Vinogradarstvo SSSR (8), 12-14 (Russian) 1981. CODEN: VIVSA6. ISSN: 0042-6318.

AB A method is described for detg. lignin substances in oak wood and cognac, based on extn. with org. solvents (acetone, CHCl3-MeOH, C6H6-EtOAc, and CHCl3-acetone), followed by TLC on silica gel and spectrophotometry. Nine lignin substances were identified: secoisolariciresinol [29388-59-8], liovil [484-39-9], lariciresinol [27003-73-2], olivil [2955-23-9], pinoresinol [487-36-5], eudesmin [526-06-7], **matairesinol** [580-72-3], **hydroxymatairesinol** [20268-71-7], and isolariciresinol [548-29-8]. The contents of each of these substances in wine increased significantly upon prolonged storage from 4.5 mg/mL (after 1 yr) to 16 mg/mL (after 20 yr).

L17 ANSWER 19 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

1978:192745 Document No.: BA66:5242. O ACYL DERIVATIVE **LIGNANS** FROM WOOD OF THE GENUS ABIES. LEONT'EVA V G; MODONOVA L D; TYUKAVKINA N A; PUNTUSOVA E G. IRKUTSK INST. ORG. CHEM., SIB. DEP., ACAD. SCI. USSR, IRKUTSK, USSR.. KHIM PRIR SOEDIN (TASHK), (1977 (RECD 1978)) (3), 337-341. CODEN: KPSUAR. ISSN: 0023-1150. Language: Russian.

AB Five new compounds were chromatographically isolated from the wood of A. sibirica and A. nephrolepis. These proved to be complex esters derivatives of the **lignans** lariciresinol, olivil and **hydroxymatairesinol**. Their structure was analyzed on the basis of spectroscopic data.

L17 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2003 ACS

1978:71443 Document No. 88:71443 **Lignan** compounds in the needles of some species of the Pinaceae family. Tyukavkina, N. A.; Medvedeva, S. A.; Ivanova, S. Z.; Lutskii, V. I. (Inst. Org. Khim., Irkutsk, USSR). Koksnes Kimija (6), 94-6 (Russian) 1977. CODEN: KHDRDQ. ISSN: 0201-7474.

AB Of the **lignans** extd. from needles of fir, spruce, larch, and pine species, secoisolariciresinol was present in all species, except those of fir; liovil, lariciresinol, **matairesinol**, and isolariciresinol were found in all species, olivil was absent in fir species, Picea ajanensis, and Larix sibirica; pinoresinol was absent in Abies sibirica and L. sibirica; **hydroxymatairesinol** was found only in spruce species; ketomatairesinol trace amts. were detected in P. koreansis only; and .alpha.-conidendrin was found in trace amts. in L. dahurica only. The total **lignan** content of needles was 0.03-0.09% (on dry-wt. basis). The needles did not contain 3,4-divanillyltetrahydrofuran, which is normally present in wood.

L17 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2003 ACS

1976:474919 Document No. 85:74919 Analysis of **lignans** in Norway Spruce by combined gas chromatography-mass spectrometry. Ekman, Rainer (Inst. Wood Chem. Cellul. Technol., Abo Akad., Abo, Finland). Holzforschung, 30(3), 79-85 (English) 1976. CODEN: HOLZAZ. ISSN: 0018-3830.

AB Me2CO-sol. **lignans** of spruce wood contained 0.5% guiaiacyl type **lignans**. The compds. identified in the ext. were isolariciresinol, secoisolariciresinol, liovil, .alpha.-conidendric acid, **lignan** A and B, lariciresinol, 2 **hydroxymatairesinol** isomers, pinoresinol, **matairesinol**, and .alpha.-conidendrin. Six unidentified **lignans** of the tetrahydrofuran series were also detected.

L17 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2003 ACS

1974:532858 Document No. 81:132858 **Lignans** from Picea koraiensis wood. Leont'eva, V. G.; Modonova, L. D.; Tyukavkina, N. A. (Irkutsk. Inst. Org. Khim., Irkutsk, USSR). Khimiya Prirodnykh Soedinenii (3), 399-400 (Russian) 1974. CODEN: KPSUAR. ISSN: 0023-1150.

AB **Lignan** contents (3,4-divanillyltetrahydrofuran, liovil,

lariciresinol, pinoresinol, ketomatairesinol, **matairesinol**, **hydroxymatairesinol**, isolariciresinol, .alpha.-conidendrin, and vanillin) in P. koraiensis, P. obovata, and P. ajanensis are tabulated. P. ajanensis contained more cyclic **lignans** than the other 2.

L17 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2003 ACS
1974:548518 Document No. 81:148518 **Lignans** from Abies sibirica wood. Leont'eva, V. G.; Modonova, L. D.; Tyukavkina, N. A. (Irkutsk. Inst. Org. Khim., Irkutsk, USSR). Izvestiya Sibirskogo Otdeleniya Akademii Nauk SSSR, Seriya Khimicheskikh Nauk (4), 158-61 (Russian) 1974. CODEN: IZSKAB. ISSN: 0002-3426.
AB The acetonic ext. fraction insol. in ligroin contained secoisolariciresinol (I), 3,4-divanilyltetrahydrofuran (II), liovil (III), lariciresinol (IV), pinoresinol (V), olivil, **matairesinol**, and **hydroxymatairesinol**. Of these, I-V were detd. for the 1st time in the wood of the Abies genus.

L17 ANSWER 24 OF 29 CAPLUS COPYRIGHT 2003 ACS
1975:141811 Document No. 82:141811 **Lignan** compounds of Siberian spruce wood (Picea obovata). Modonova, L. D.; Tyukavkina, N. A. (Irkutsk. Inst. Org. Khim., Irkutsk, USSR). Khim. Ispol'z. Lignina, 73-86. Editor(s): Sergeev, V. N. "Zinatne": Riga, USSR. (Russian) 1974. CODEN: 29THA7.
AB The extn. of Picea obovata with MeOH or acetone gave 8.8 or 8.7% (on dry wood wt.) resp. of phenolic constituents. These compds. were sepd. by thin layer chromatog. and identified as conidendrin [518-55-8], 3,4-divanillyltetrahydrofuran [34730-78-4], pinoresinol [487-36-5], **matairesinol** [580-72-3], ketomatairesinol [53250-61-6], lariciresinol [27003-73-2], **hydroxymatairesinol** [20268-71-7], and liovil [484-39-9]. The wood of Picea obovata had low resistance to fungus infection. Biol. testing showed that none of the above-indicated **lignans** had any fungicidal properties.

L17 ANSWER 25 OF 29 CAPLUS COPYRIGHT 2003 ACS
1975:74652 Document No. 82:74652 **Lignans** from Abies nephrolepis and Picea ajanensis. Leont'eva, V. G.; Modonova, L. D.; Tyukovkina, N. A. (Irkutsk. Inst. Org. Khim., Irkutsk, USSR). Khimiya Prirodnykh Soedinenii (2), 268-9 (Russian) 1973. CODEN: KPSUAR. ISSN: 0023-1150.
AB The phenolic substances, extd. from Picea ajanensis with acetone, include .alpha.-conidendrin [518-55-8], **matairesinol** (I) [580-72-3], ketomatairesinol, **hydroxymatairesinol** (II) 3,4-divinyltetrahydrofuran (III) [41233-91-4], (+)-pinoresinol (IV) [487-36-5], liovil (V) [484-39-9], isolariciresinol [548-29-8], vanillin (VI) [121-33-5], and vanillic acid [121-34-6]. The exts. from Abies nephrolepis contain I-VI. The substances were sepd. by chromatog. on powd. polyamide and silica gel impregnated with 2% Na metabisulfite soln.

L17 ANSWER 26 OF 29 CAPLUS COPYRIGHT 2003 ACS
1973:99363 Document No. 78:99363 Isolation of two **lignans** from Ezomatsu (Picea jezoensis). Omori, Shigetoshi; Sakakibara, Akira (Fac. Agric., Hokkaido Univ., Sapporo, Japan). Mokuzai Gakkaishi, 19(1), 41-4 (Japanese) 1973. CODEN: MKZGA7. ISSN: 0021-4795.
AB The title wood meal was extd. with 1:2 EtOH-benzene, concd., and extd. with petroleum ether to give (-)-.alpha.-conidendrin (I) [518-55-8] and (-)-**hydroxymatairesinol** (II).

L17 ANSWER 27 OF 29 CAPLUS COPYRIGHT 2003 ACS
1971:506237 Document No. 75:106237 Phenolic extractives in Norway spruce and their effects on Fomes annosus. Shain, Louis; Hillis, W. E. (Div. Forest Prod., CSIRO, South Melbourne, Australia). Phytopathology, 61(7), 841-5 (English) 1971. CODEN: PHYTAJ. ISSN: 0031-949X.
GI For diagram(s), see printed CA Issue.

AB **Hydroxymatairesinol** (I), **matairesinol**, liovil, and conidendrin were identified in healthy heartwood tissue of Norway spruce (Picea abies) as well as in the reaction zone sepg. healthy sapwood from wood decayed by F. annosus. The reaction zone contained considerably more I than was found in heartwood. Healthy sapwood and wood in advanced stages of decay contained negligible quantities of **lignans**. I was significantly more inhibitory to F. annosus than was matariresinol or conidendrin in vitro. I in assocn. with the alkalinity in the reaction zone may contribute to the resistance of the sapwood to F. annosus in vivo.

L17 ANSWER 28 OF 29 CAPLUS COPYRIGHT 2003 ACS

1970:511114 Document No. 73:111114 Cellular distribution of **lignans** in Tsuga heterophylla wood. Krahmer, R. L.; Hemingway, R. W.; Hillis, W. E. (Forest Prod. Lab., C.S.I.R.O., South Melbourne, Australia). Wood Science and Technology, 4(2), 122-39 (English) 1970. CODEN: WOSTBE. ISSN: 0043-7719.

AB Western hemlock heartwood contained tracheids with large amts. of cellular inclusions and deposits contg. the **lignans matairesinol**, **hydroxymatairesinol**, and conidendrin. The deposits occurred in 3 different forms and various chem. compns. Rays contained deposits phys. similar to those in adjacent tracheids, but did not contain **lignans**, although **lignans** were present in the tracheids. **Lignans** formed surface films on tracheid walls and encrusted the bordered pits. The amt. of **lignans** was not related to wet wood zones. The **lignan** biosynthesis probably occurred in the heartwood periphery in the vicinity of the half-bordered pits.

L17 ANSWER 29 OF 29 CAPLUS COPYRIGHT 2003 ACS

1958:88001 Document No. 52:88001 Original Reference No. 52:15494c-i,15495a-i,15496a-c The **lignans** of fir wood. Freudenberg, Karl; Knof, Leo (Univ. Heidelberg, Germany). Chem. Ber., 90, 2957-69 (Unavailable) 1957.

AB A 20-30 years old fir freed of its bark and dried, resin-free pieces reduced to saw dust, 4-kg. portions air-dried saw dust each in three 16-1. percolators extd. with 85% aq. Me2CO, the 1st 20 l. percolate from the 1st percolator passed through the 2nd and 3rd percolator during 10 days, the percolate from a total of 40 kg. wood evapd. in vacuo, the tacky residue (637 g.) added to 400 cc. anhyd. Me2CO, the resulting 2 phases centrifuged from a small amt. of solid, the 2-phase supernatant evapd. in vacuo, a 100-g. portions of the solid residue dissolved in 100 cc. 4:1 HCONH2-H2O, the soln. washed with three 60-cc. portions Et2O, and the Et2O washing and the aq. soln. subjected to a countercurrent distribution with 1:3 HCONH2-H2O (satd. with Et2O) yielded the following fractions (designation of fraction, tube no., color of coupling product with diazotized sulfanilic acid in 2% aq. Na2CO3, % of charge, and main components given): A, up to 238, almost none, 29.3, phenol-free material; B, 239-660, red, 9.5, red-coupling **lignans**; C, 661-1278, yellow, 16.2, **hydroxymatairesinols**; D, 1279-2100, yellow, 3.6, liovil (I); E, 2101-2380 and 120-200, yellow, 2.5, yellow-coupling substances; F, 70-119, yellow, 1.7, yellow-coupling substances; G, 35-69, yellow, 3.3, yellow-coupling substances; H, 1-34, yellow, 9.6, dissolved lignin portion; I, 1-34, yellow, 20.3, undissolved lignin portion. The phenol free resin fraction A (60 g.) distd. at 0.4 mm. to 300.degree. gave 35 g. distillate which redistd. yielded 14 g. distillate, b0.01 to 180.degree., and 15 g. distillate, b0.01 180-98.degree.. The first distillate fraction hydrogenated gave 4.5 g. stearic acid. Fraction B (37 g.) gave after removal of the Et2O 5 g. cryst. (-)-.alpha.-conidendrin (II), m. 238.degree. with resolidification and rem. 256.degree. (HCO2H and EtOH), [.alpha.]25D -71.4.degree. (c 4, tetrahydrofuran), -54.5.degree. (Me2CO); II freshly recrystd. from HCO2H showed sometimes a m.p. of 242-3.degree. with resolidiflcation and rem. 262-3.degree.. The mother liquor from the

II evapd., the residue dissolved in tetrahydrofuran, the soln. evapd., the residue (31 g.) redissolved in 80 cc. HCONH2, and the soln. subjected to a countercurrent distribution with 1:1 HCONH2-H2O (satd. with Et2O) yielded the following fractions (same data given): B-1, to 347, almost none, 6, phenol-free materials; B-2, 348-447, lemon-yellow with blue fluorescence, 7, coniferylaldehyde (III) with little 3,4-divanillyltetrahydrofuran (IV) and vanillin (V); B-3, 448-687, red, 21, pinoresinol (VI) and **matairesinol** (VII); B-4, 688-1005, gray-red, 20, II with a little VII; B-5, 1000-1349, red-violet, 14, oxomatairesinol (VIII) and II; B-6, 1350-1728, red, 9, lariciresinol (IX) with a little II; B-7, 1729-1915 and 160-200, red, 4, II with a little **hydroxymatairesinols**; B-8, 100-159, yellow, 7, **hydroxymatairesinols**; B-9, 1-99, yellow, 2, -. Fraction B-2 in EtOH treated with KOAc in EtOH, the adduct treated with H2O contg. a small amt. of hydroquinone and filtered, and the residue dried and recrystd. from C6H6 contg. a trace of hydroquinone gave III; 2,4-dinitrophenylhydrazone, m. 266-9.degree.. The filtrate from the adduct evapd., the residue treated with CH2Cl2 and H2O, the org. layer evapd., and the residue dissolved in EtOH and treated with 3 g. 2,4-(O2N)2C6H3NHNH2 in 100 cc. EtOH and 2 cc. concd. HCl gave the 2,4-dinitrophenylhydrazone of V, m. 266-7.degree.. The presence of IV in fraction B-2 was demonstrated by the paper chromatogram. Fraction B-3 (3.5 g.) ground with 6 cc. satd. alc. KOAc, allowed to stand 6 hrs., and filtered, and the residue washed with alc. KOAc and decompd. with CH2Cl2 and H2O yielded 1.4 g. (crude) (+)-VI, m. 119-20.degree. (EtOH), contg. 13% (.+-.)-VI, which recrystd. further gave 94%-pure (+)-VI, [.alpha.]21D 84.4.degree. (c 5, Me2CO). Fraction B-3 (4 g.) combined with 2 g. residue from the isolation of the VI and dissolved in 50 cc. CHCl3, and the soln. subjected to a 495-transfer countercurrent distribution yielded in the tubes 142-192 1.26 g. (crude) (-)-VII, m. 116-18.degree. (30% aq. AcOH), [.alpha.]25D -45.0.degree. (c 4.2, Me2CO); di-Me ether, m. 129-30.degree., [.alpha.]25D -31.8.degree. (c 1.7, CHCl3). Fraction B-4 digested with a little AmOH and filtered gave II. Fraction B-5 (4 g.) in 25 cc. CHCl3 subjected to a 375-transfer countercurrent distribution with 3:2.5:6 HCONH2-H2OCHCl3 yielded in tubes 80-118 2 g. (+)-VIII, m. 70-2.degree., [.alpha.]25D 42.6.degree. (c 4.0, tetrahydrofuran) (diacetate, needles, m. 122-3.degree. (EtOH)], and in tubes 20-42 0.8 g. II. VIII in EtOAc hydrogenated in the presence of PdCl2 yielded VII, m. 116-17.degree., [.alpha.]25D -45.1.degree. (c Me2CO). VIII in EtOAc hydrogenated 2 days over 5% Pd-kieselguhr gave in addn. to VII and VIII also (-)-**hydroxymatairesinol** (X), and (-)-allohydroxymatairesinol (XI); the crude product treated with alc. KOAc gave the X-KOAc adduct, m. 120-2.degree.. Fraction B-6 crystd. partially to deposit IX. The combined fractions C and B-8 (10 g.)in 15 cc. HCONH2 and 3 cc. H2O subjected to a 2630-transfer countercurrent distribution with 1:3.5:5 HCONH2-H2O-CHCl3 gave 2.7 g.-amorphous X, [.alpha.]22D -11.0.degree. (c 4.0, tetrahydrofuran), -6.3.degree. (c 4, EtOH), and 4.0 g. XI, [.alpha.]25D -9.8.degree. (c 4.0, tetrahydrofuran), 4.9.degree. (c 4, EtOH). A mixt. (10 g.) of X and XI kept 1 day at 20.degree. with 10 cc. satd. alc. KOAc and filtered, and the residue washed with a little PrOH yielded 6.5 g. X-KOAc adduct, m. 126-7.degree. (BuOH). X gave also with PrOH satd. with EtCO2K a cryst. adduct. X-KOAc adduct (6 g.) dissolved in a few cc. 2:3 Me2CO-H2O, shaken with 70 cc. H2O and 75 cc. CH2Cl2, the aq. layer extd. with CH2Cl2, and the combined CH2Cl2 solns. evapd. while protected from light gave 4.4 g. colorless residue; X-XI mixt. heated with alc. KOAc yielded with the disappearance of the X-XI apparently higher mol. wt. orange-yellow coupling material. X (1 g.) dissolved in 60.degree. in 1 g. NaOH in 1 cc. H2O, cooled, neutralized with 50% AcOH, cooled with ice, and filtered, the residue washed with dil. aq. NaOAc, dissolved in 10 cc. MeOH, and the soln. dild. with 15 cc. C6H6 gave 0.3 g. Na (-)-hydroxymatairesinolate, prisms, which acidified with moderately dil. AcOH gave oily crystals. X with 2,4-(O2N)2C6H3F gave a yellow amorphous powder which subjected to countercurrent distribution with

5:3.5:1.5, CH2Cl2-MeOH-H2O, then with 3:2:1:0.6, and finally with 5:4.5:1.5:1 HCONMe2-C6H6-cyclohexane-H2O yielded the 2,4-dinitrophenyl ether deriv. of X, amorphous solid; acetate, amorphous solid. X with CH2N2 gave the di-Me ether, m. 96-7.degree. (AmOH), [.alpha.]25D 59.8.degree. (c 2.0, tetrahydrofuran). X (0.5 g.) in EtOAc hydrogenated over 0.2 g. Pd during 16 hrs., filtered, and evapd., and the residue recrystd. from 3:7 glacial AcOH-H2O yielded 71% (-)-VII. XI gave similarly 50% (-)-VII. II converted to the di-Me ether and then treated with Pb(OAc)2 gave a phenylnaphthalene deriv., m. 216-17.degree. with resolidification and rem. 225-7.degree.. X (0.20 g.) in 5 cc. of a soln. of 1 cc. concd. H2SO4 in 20 cc. tetrahydrofuran showed the following [.alpha.]25D values at the times in min. given in parentheses: -6.1.degree. (10), 1.4.degree. (35), 11.7.degree. (105), 19.0.degree. (260), 19.4.degree. (290), 3.1.degree. (1185), -1.7.degree. (1415), -21.6.degree. (2520), -42.4.degree. (4140), -56.8.degree. (5950), -58.0.degree. (6000). This change of rotation indicates a conversion of X to II. Fraction D (3.5 g.) digested with 8 cc. AmOH, refrigerated 18 hrs., and filtered gave 0.8 g. (-)-I, prisms, m. 173.5-4.5.degree. (aq. MeOH), [.alpha.]25D -32.8.degree. (c 4.0, MeOH); tetraacetate, m. 124-5.degree. (EtOH). The AmOH ext. from fraction D evapd., the residue dissolved warm in 375 cc. CHCl3 and 375 cc. H2O, and the mixt. subjected to a 185-transfer countercurrent distribution gave in tubes 90-125 an addnl. 0.36 g. (-)-I. (-)-I (0.25 g.) in EtOAc hydrogenated 2 days over 0.2 g. Pd black gave IV, prisms, m. 116-17.degree. (Me3COH), [.alpha.]25D -52.2.degree. (c 1.4, tetrahydrofuran). VI in EtOAc hydrogenated 1.5 hrs. over prehydrogenated PdCl2 and the mixt. chromatographed on paper showed the presence of VI, IX, and 2,3-divanillyl-1,4-butanediol, Rf 0.85 (HCONH2-Et2O), which coupled with a red-violet color; the mixt. dehydrated by the method of Haworth and Woodcock (C.A. 33, 68332) yielded 35% IV, m. 116-17.degree.. (+)-IX hydrogenated in EtOAc in the usual manner yielded during 40 min. 70% IV, [.alpha.]25D -51.8.degree. (c 4.0, tetrahydrofuran). IV showed the following Rf values with the listed solvents satd. with HCONH2: Et2O 0.67, CHCl3 0.91, CHCl:CCl2 0.67, PhCl 0.66, C6H6 0.61, CCl4 0.35, cyclohexane 0.02. IX showed under the same conditions the following Rf values: Et2O 0.14, CHCl3 0.38, PhCl 0.04, C6H6 0.03, CH2Cl2 0.34. IV showed the following Rf values with the listed solvents half-satd. with HCONH2: MECH-(OMe)2 0.68, MeCH(OEt)2 0.64. IX showed under the same conditions the following Rf values: MeCH(OMe)2 0.43, MeCH(OEt)2 0.18 ,CH2Cl2 0.41. The Rm values (cf. Brooks, et al., C.A. 51, 12113d) were detd. for the following compds.: dehydrodiisoeugenol -0.85, dehydrodiconiferyl alc. 0.91, X 1.00, VII 0.25, I 1.28, IV -0.25, VIII 0.63, II 0.42. From these values were calcd. the following Rf group increments: OH (.gamma.) 0.88, OH (.alpha.) 0.75, OH (.alpha.) 0.76, .alpha.-oxo group 0.38, ring closure with the loss of 2H 0.17. The red coupling amorphous trace amts. (accompanying II in fraction B) with Rf 0.54-0.55 might possibly be 2,5-diguaiacyl-3,4-dimethyltetrahydrofuran for which an Rf value of 0.54 is calcd.

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=> s (ahotupa m?/au or eriksson j?/au or kangas l?/au or komi j?/au or perala m?/au
or korte h?/au)
L18        3541 (AHOTUPA M?/AU OR ERIKSSON J?/AU OR KANGAS L?/AU OR KOMI J?/AU
                OR PERALA M?/AU OR KORTE H?/AU)

=> s l18 and lignan
L19          10 L18 AND LIGNAN

=> dup remove l19
PROCESSING COMPLETED FOR L19
L20           4 DUP REMOVE L19 (6 DUPLICATES REMOVED)

=> d l20 1-4 cbib abs
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L20 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
2002:392225 Document No. 136:380145 Prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases by use of hydroxymatairesinol, and a pharmaceutical preparation, food additive and food product comprising hydroxymatairesinol. **Ahotupa, Markku;** Eckerman, Christer; **Kangas, Lauri;** Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni (Finland). U.S. Pat. Appl. Publ. US 2002061854 A1 20020523, 15 pp., Cont.-in-part of U.S. Ser. No. 829,944. (English). CODEN: USXXCO. APPLICATION: US 2001-972850 20011010. PRIORITY: US 1999-281094 19990330; US 2001-829944 20010411.

AB The invention discloses methods for prevention of cancers, certain non-cancerous, hormone-dependent diseases, and/or cardiovascular diseases in a person, based on the administration of hydroxymatairesinol. The invention also discloses a method for increasing the level of enterolactone or another metabolite of hydroxymatairesinol in a person's serum, thereby causing prevention of a cancer or a certain non-cancerous, hormone-dependent disease in a person, based on administration of hydroxymatairesinol. Furthermore, the invention discloses pharmaceutical prepns., food additives, and food products comprising hydroxymatairesinol.

L20 ANSWER 2 OF 4 MEDLINE DUPLICATE 1
2003059990 Document Number: 22457755. PubMed ID: 12570335. Antioxidant and antitumor effects of hydroxymatairesinol (HM-3000, HMR), a **lignan** isolated from the knots of spruce. **Kangas Lauri;** Saarinen Niina; Mutanen Marja; **Ahotupa Markku;** Hirsinummi Riikka; Unkila Mikko; **Perala Merja;** Soininen Pasi; Laatikainen Reino; **Korte Helena;** Santti Risto. (Hormos Nutraceutical Ltd, Turku, Finland.) EUROPEAN JOURNAL OF CANCER PREVENTION, (2002 Aug) 11 Suppl 2 S48-57. Journal code: 9300837. ISSN: 0959-8278. Pub. country: England: United Kingdom. Language: English.

AB The antioxidant properties of hydroxymatairesinol (HM-3000) were studied in vitro in lipid peroxidation, superoxide and peroxyl radical scavenging, and LDL-oxidation models in comparison with the known synthetic antioxidants Trolox (a water-soluble vitamin E derivative), butylated hydroxyanisol (BHA) and butylated hydroxytoluene (BHT). On a molar basis HM-3000 was a more effective antioxidant than Trolox in all assays and more effective than BHT or BHA in lipid peroxidation and superoxide scavenging test. The in vivo antioxidative effect (evaluated as the weight gain of C57BL/6J mice fed an alpha-tocopherol-deficient diet) of HM-3000 (500 mg/kg per day) was comparable to that of DL-alpha-tocopherol (766 mg/kg per day). The antitumor activity of HM-3000 was studied in dimethylbenz[a]anthracene (DMBA)-induced rat mammary cancer. HM-3000 had a statistically significant inhibitory effect on tumor growth. Prevention of tumor formation was also evaluated in the Apc(Min) mice model, which develops intestinal polyps spontaneously. HM-3000 was given in diet at 30 mg/kg per day and decreased the formation of polyps and prevented beta-catenin accumulation into the nucleus, the pathophysiological hallmark of polyp formation in this mouse model. In short-term toxicity studies (up to 28 days) HM-3000 was essentially non-toxic when given p.o. to rats and dogs (daily doses up to 2000 and 665 mg/kg, respectively); HM-3000 was shown to be well absorbed (> 50% of the dose) and rapidly eliminated. In human studies HM-3000 has been given in single doses up to 1350 mg to healthy male volunteers without treatment-related adverse events. Rapid absorption from the gastrointestinal tract and partial metabolism to enterolactone in humans was demonstrated. In summary, HM-3000 is a safe, novel enterolactone precursor **lignan** with antioxidant and antitumor properties.

L20 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS
2000:725669 Document No. 133:286508 Hydroxymatairesinol preparations in cancer prevention. **Ahotupa, Markku;** Eckerman, Christer;

Kangas, Lauri; Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni (Hormos Nutraceutical Oy Ltd., Finland). PCT Int. Appl. WO 2000059946 A1 20001012, 43 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-FI181 20000309. PRIORITY: US 1999-281094 19990330.

AB This invention relates to methods for prevention of cancers, certain non-cancer, hormone dependent diseases and/or cardiovascular diseases in a person, based on administering of hydroxymatairesinol to said person. The invention also concerns a method for increasing the level of enterolactone or another metabolite of hydroxymatairesinol in a person's serum thereby causing prevention of a cancer or a certain non-cancer, hormone dependent disease in a person, based on administering of hydroxymatairesinol to said person. Furthermore, this invention relates to pharmaceutical prepns., food additives and food products comprising hydroxymatairesinol.

L20 ANSWER 4 OF 4 MEDLINE DUPLICATE 2

2001103469 Document Number: 20348508. PubMed ID: 10890032.
Hydroxymatairesinol, a novel enterolactone precursor with antitumor properties from coniferous tree (Picea abies). Saarinen N M; Warri A; Makela S I; Eckerman C; Reunanen M; **Ahotupa M**; Salmi S M; Franke A A; **Kangas L**; Santti R. (Department of Anatomy, University of Turku, Finland.) NUTRITION AND CANCER, (2000) 36 (2) 207-16. Journal code: 7905040. ISSN: 0163-5581. Pub. country: United States. Language: English.

AB The potential for the extraction of the plant **lignan** hydroxymatairesinol (HMR) in large scale from Norway spruce (Picea abies) has given us the opportunity to study the metabolism and biological actions of HMR in animals. HMR, the most abundant single component of spruce **lignans**, was metabolized to enterolactone (ENL) as the major metabolite in rats after oral administration. The amounts of urinary ENL increased with the dose of HMR (from 3 to 50 mg/kg), and only minor amounts of unmetabolized HMR isomers and other **lignans** were found in urine. HMR (15 mg/kg body wt po) given for 51 days decreased the number of growing tumors and increased the proportion of regressing and stabilized tumors in the rat dimethylbenz[a]anthracene-induced mammary tumor model. HMR (50 mg/kg body wt) did not exert estrogenic or antiestrogenic activity in the uterine growth test in immature rats. HMR also showed no antiandrogenic responses in the growth of accessory sex glands in adult male rats. Neither ENL nor enterodiol showed estrogenic or antiestrogenic activity via a classical alpha- or beta-type estrogen receptor-mediated pathway in vitro at < 1.0 microM. HMR was an effective antioxidant in vitro.

=> s l18 and hydroxymatairesinol
L21 11 L18 AND HYDROXYMATAIRESINOL

=> dup remove l21
PROCESSING COMPLETED FOR L21
L22 5 DUP REMOVE L21 (6 DUPLICATES REMOVED)

=> d l22 1-5 cbib abs

L22 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
2002:583081 Document No.: PREV200200583081. USE OF **HYDROXYMATAIRESINOL** FOR PREVENTION OF CANCERS, NON-CANCER, HORMONE DEPENDENT DISEASES AND

CARDIOVASCULAR DISEASES BY **HYDROXYMATAIRESINOL**, AND A PHARMACEUTICAL PREPARATION, FOOD ADDITIVE AND FOOD PRODUCT COMPRISING **HYDROXYMATAIRESINOL**. **Ahotupa, Markku (1)**; Eckerman, Chester; **Kangas, Lauri**; Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni. (1) Turku Finland. ASSIGNEE: Hormos Nutraceutical Oy Ltd., Turku, Finland. Patent Info.: US 6451849 September 17, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 17, 2002) Vol. 1262, No. 3, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133. Language: English.

AB This invention relates to methods for prevention of cancers, certain non-cancer, hormone dependent diseases and/or cardiovascular diseases in a person, based on administering of **hydroxymatairesinol** to said person. The invention also concerns a method for increasing the level of enterolactone or another metabolite of **hydroxymatairesinol** in a person's serum thereby causing prevention of a cancer or a certain non-cancer, hormone dependent disease in a person, based on administering of **hydroxymatairesinol** to said person. Furthermore, this invention relates to pharmaceutical preparations, food additives and food products comprising **hydroxymatairesinol**.

L22 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS

2002:392225 Document No. 136:380145 Prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases by use of **hydroxymatairesinol**, and a pharmaceutical preparation, food additive and food product comprising **hydroxymatairesinol**. **Ahotupa, Markku**; Eckerman, Christer; **Kangas, Lauri**; Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni (Finland). U.S. Pat. Appl. Publ. US 2002061854 A1 20020523, 15 pp., Cont.-in-part of U.S. Ser. No. 829,944. (English). CODEN: USXXCO. APPLICATION: US 2001-972850 20011010. PRIORITY: US 1999-281094 19990330; US 2001-829944 20010411.

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L22 ANSWER 3 OF 5 MEDLINE DUPLICATE 1

2003059990 Document Number: 22457755. PubMed ID: 12570335. Antioxidant and antitumor effects of **hydroxymatairesinol** (HM-3000, HMR), a lignan isolated from the knots of spruce. **Kangas Lauri**; Saarinen Niina; Mutanen Marja; **Ahotupa Markku**; Hirsinummi Riikka; Unkila Mikko; **Perala Merja**; Soininen Pasi; Laatikainen Reino; **Korte Helena**; Santti Risto. (Hormos Nutraceutical Ltd, Turku, Finland.) EUROPEAN JOURNAL OF CANCER PREVENTION, (2002 Aug) 11 Suppl 2 S48-57. Journal code: 9300837. ISSN: 0959-8278. Pub. country: England: United Kingdom. Language: English.

AB The antioxidant properties of **hydroxymatairesinol** (HM-3000) were studied in vitro in lipid peroxidation, superoxide and peroxyl radical scavenging, and LDL-oxidation models in comparison with the known synthetic antioxidants Trolox (a water-soluble vitamin E derivative), butylated hydroxyanisol (BHA) and butylated hydroxytoluene (BHT). On a molar basis HM-3000 was a more effective antioxidant than Trolox in all assays and more effective than BHT or BHA in lipid peroxidation and superoxide scavenging test. The in vivo antioxidative effect (evaluated as the weight gain of C57BL/6J mice fed an alpha-tocopherol-deficient diet) of HM-3000 (500 mg/kg per day) was comparable to that of

DL-alpha-tocopherol (766 mg/kg per day). The antitumor activity of HM-3000 was studied in dimethylbenz[a]anthracene (DMBA)-induced rat mammary cancer. HM-3000 had a statistically significant inhibitory effect on tumor growth. Prevention of tumor formation was also evaluated in the Apc(Min) mice model, which develops intestinal polyps spontaneously. HM-3000 was given in diet at 30 mg/kg per day and decreased the formation of polyps and prevented beta-catenin accumulation into the nucleus, the pathophysiological hallmark of polyp formation in this mouse model. In short-term toxicity studies (up to 28 days) HM-3000 was essentially non-toxic when given p.o. to rats and dogs (daily doses up to 2000 and 665 mg/kg, respectively); HM-3000 was shown to be well absorbed (> 50% of the dose) and rapidly eliminated. In human studies HM-3000 has been given in single doses up to 1350 mg to healthy male volunteers without treatment-related adverse events. Rapid absorption from the gastrointestinal tract and partial metabolism to enterolactone in humans was demonstrated. In summary, HM-3000 is a safe, novel enterolactone precursor lignan with antioxidant and antitumor properties.

L22 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS
2000:725669 Document No. 133:286508 **Hydroxymatairesinol** preparations in cancer prevention. **Ahotupa, Markku;** Eckerman, Christer; **Kangas, Lauri;** Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni (Hormos Nutraceutical Oy Ltd., Finland). PCT Int. Appl. WO 2000059946 A1 20001012, 43 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-FI181 20000309. PRIORITY: US 1999-281094 19990330.

AB This invention relates to methods for prevention of cancers, certain non-cancer, hormone dependent diseases and/or cardiovascular diseases in a person, based on administering of **hydroxymatairesinol** to said person. The invention also concerns a method for increasing the level of enterolactone or another metabolite of **hydroxymatairesinol** in a person's serum thereby causing prevention of a cancer or a certain non-cancer, hormone dependent disease in a person, based on administering of **hydroxymatairesinol** to said person. Furthermore, this invention relates to pharmaceutical prepns., food additives and food products comprising **hydroxymatairesinol**.

L22 ANSWER 5 OF 5 MEDLINE DUPLICATE 2
2001103469 Document Number: 20348508. PubMed ID: 10890032.
Hydroxymatairesinol, a novel enterolactone precursor with antitumor properties from coniferous tree (Picea abies). Saarinen N M; Warri A; Makela S I; Eckerman C; Reunanen M; **Ahotupa M;** Salmi S M; Franke A A; **Kangas L;** Santti R. (Department of Anatomy, University of Turku, Finland.) NUTRITION AND CANCER, (2000) 36 (2) 207-16. Journal code: 7905040. ISSN: 0163-5581. Pub. country: United States. Language: English.

AB The potential for the extraction of the plant lignan **hydroxymatairesinol** (HMR) in large scale from Norway spruce (Picea abies) has given us the opportunity to study the metabolism and biological actions of HMR in animals. HMR, the most abundant single component of spruce lignans, was metabolized to enterolactone (ENL) as the major metabolite in rats after oral administration. The amounts of urinary ENL increased with the dose of HMR (from 3 to 50 mg/kg), and only minor amounts of unmetabolized HMR isomers and other lignans were found in urine. HMR (15 mg/kg body wt po) given for 51 days decreased the number of growing tumors and increased the proportion of regressing and

stabilized tumors in the rat dimethylbenz[a]anthracene-induced mammary tumor model. HMR (50 mg/kg body wt) did not exert estrogenic or antiestrogenic activity in the uterine growth test in immature rats. HMR also showed no antiandrogenic responses in the growth of accessory sex glands in adult male rats. Neither ENL nor enterodiol showed estrogenic or antiestrogenic activity via a classical alpha- or beta-type estrogen receptor-mediated pathway in vitro at < 1.0 microM. HMR was an effective antioxidant in vitro.

=> s l18 and matairesinol
L23 2 L18 AND MATAIRESINOL

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PROCESSING COMPLETED FOR L23
L24 1 DUP REMOVE L23 (1 DUPLICATE REMOVED)

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L24 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
2001103469 Document Number: 20348508. PubMed ID: 10890032.
Hydroxymatairesinol, a novel enterolactone precursor with antitumor properties from coniferous tree (Picea abies). Saarinen N M; Warri A; Makela S I; Eckerman C; Reunanen M; **Ahotupa M**; Salmi S M; Franke A A; **Kangas L**; Santti R. (Department of Anatomy, University of Turku, Finland.) NUTRITION AND CANCER, (2000) 36 (2) 207-16. Journal code: 7905040. ISSN: 0163-5581. Pub. country: United States. Language: English.
AB The potential for the extraction of the plant lignan hydroxymatairesinol (HMR) in large scale from Norway spruce (Picea abies) has given us the opportunity to study the metabolism and biological actions of HMR in animals. HMR, the most abundant single component of spruce lignans, was metabolized to enterolactone (ENL) as the major metabolite in rats after oral administration. The amounts of urinary ENL increased with the dose of HMR (from 3 to 50 mg/kg), and only minor amounts of unmetabolized HMR isomers and other lignans were found in urine. HMR (15 mg/kg body wt po) given for 51 days decreased the number of growing tumors and increased the proportion of regressing and stabilized tumors in the rat dimethylbenz[a]anthracene-induced mammary tumor model. HMR (50 mg/kg body wt) did not exert estrogenic or antiestrogenic activity in the uterine growth test in immature rats. HMR also showed no antiandrogenic responses in the growth of accessory sex glands in adult male rats. Neither ENL nor enterodiol showed estrogenic or antiestrogenic activity via a classical alpha- or beta-type estrogen receptor-mediated pathway in vitro at < 1.0 microM. HMR was an effective antioxidant in vitro.

=> s l18 and enterolactone
L25 11 L18 AND ENTEROLACTONE

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PROCESSING COMPLETED FOR L25
L26 5 DUP REMOVE L25 (6 DUPLICATES REMOVED)

=> d l26 1-5 cbib abs

L26 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
2002:583081 Document No.: PREV200200583081. USE OF HYDROXYMATAIRESINOL FOR PREVENTION OF CANCERS, NON-CANCER, HORMONE DEPENDENT DISEASES AND CARDIOVASCULAR DISEASES BY HYDROXYMATAIRESINOL, AND A PHARMACEUTICAL PREPARATION, FOOD ADDITIVE AND FOOD PRODUCT COMPRISING HYDROXYMATAIRESINOL. **Ahotupa, Markku (1)**; Eckerman, Chester;

Kangas, Lauri; Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni. (1) Turku Finland. ASSIGNEE: Hormos Nutraceutical Oy Ltd., Turku, Finland. Patent Info.: US 6451849 September 17, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 17, 2002) Vol. 1262, No. 3, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133. Language: English.

AB This invention relates to methods for prevention of cancers, certain non-cancer, hormone dependent diseases and/or cardiovascular diseases in a person, based on administering of hydroxymatairesinol to said person. The invention also concerns a method for increasing the level of **enterolactone** or another metabolite of hydroxymatairesinol in a person's serum thereby causing prevention of a cancer or a certain non-cancer, hormone dependent disease in a person, based on administering of hydroxymatairesinol to said person. Furthermore, this invention relates to pharmaceutical preparations, food additives and food products comprising hydroxymatairesinol.

L26 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS

2002:392225 Document No. 136:380145 Prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases by use of hydroxymatairesinol, and a pharmaceutical preparation, food additive and food product comprising hydroxymatairesinol. **Ahotupa, Markku**; Eckerman, Christer; **Kangas, Lauri**; Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni (Finland). U.S. Pat. Appl. Publ. US 2002061854 A1 20020523, 15 pp., Cont.-in-part of U.S. Ser. No. 829,944. (English). CODEN: USXXCO. APPLICATION: US 2001-972850 20011010. PRIORITY: US 1999-281094 19990330; US 2001-829944 20010411.

AB The invention discloses methods for prevention of cancers, certain non-cancerous, hormone-dependent diseases, and/or cardiovascular diseases in a person, based on the administration of hydroxymatairesinol. The invention also discloses a method for increasing the level of **enterolactone** or another metabolite of hydroxymatairesinol in a person's serum, thereby causing prevention of a cancer or a certain non-cancerous, hormone-dependent disease in a person, based on administration of hydroxymatairesinol. Furthermore, the invention discloses pharmaceutical prepns., food additives, and food products comprising hydroxymatairesinol.

L26 ANSWER 3 OF 5 MEDLINE DUPLICATE 1

2003059990 Document Number: 22457755. PubMed ID: 12570335. Antioxidant and antitumor effects of hydroxymatairesinol (HM-3000, HMR), a lignan isolated from the knots of spruce. **Kangas Lauri**; Saarinen Niina; Mutanen Marja; **Ahotupa Markku**; Hirsinummi Riikka; Unkila Mikko; **Perala Merja**; Soininen Pasi; Laatikainen Reino; **Korte Helena**; Santti Risto. (Hormos Nutraceutical Ltd, Turku, Finland.) EUROPEAN JOURNAL OF CANCER PREVENTION, (2002 Aug) 11 Suppl 2 S48-57. Journal code: 9300837. ISSN: 0959-8278. Pub. country: England: United Kingdom. Language: English.

AB The antioxidant properties of hydroxymatairesinol (HM-3000) were studied in vitro in lipid peroxidation, superoxide and peroxyl radical scavenging, and LDL-oxidation models in comparison with the known synthetic antioxidants Trolox (a water-soluble vitamin E derivative), butylated hydroxyanisol (BHA) and butylated hydroxytoluene (BHT). On a molar basis HM-3000 was a more effective antioxidant than Trolox in all assays and more effective than BHT or BHA in lipid peroxidation and superoxide scavenging test. The in vivo antioxidative effect (evaluated as the weight gain of C57BL/6J mice fed an alpha-tocopherol-deficient diet) of HM-3000 (500 mg/kg per day) was comparable to that of DL-alpha-tocopherol (766 mg/kg per day). The antitumor activity of HM-3000 was studied in dimethylbenz[a]anthracene (DMBA)-induced rat mammary cancer. HM-3000 had a statistically significant inhibitory effect on tumor growth. Prevention

of tumor formation was also evaluated in the Apc(Min) mice model, which develops intestinal polyps spontaneously. HM-3000 was given in diet at 30 mg/kg per day and decreased the formation of polyps and prevented beta-catenin accumulation into the nucleus, the pathophysiological hallmark of polyp formation in this mouse model. In short-term toxicity studies (up to 28 days) HM-3000 was essentially non-toxic when given p.o. to rats and dogs (daily doses up to 2000 and 665 mg/kg, respectively); HM-3000 was shown to be well absorbed (> 50% of the dose) and rapidly eliminated. In human studies HM-3000 has been given in single doses up to 1350 mg to healthy male volunteers without treatment-related adverse events. Rapid absorption from the gastrointestinal tract and partial metabolism to **enterolactone** in humans was demonstrated. In summary, HM-3000 is a safe, novel **enterolactone** precursor lignan with antioxidant and antitumor properties.

L26 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS
2000:725669 Document No. 133:286508 Hydroxymatairesinol preparations in cancer prevention. **Ahotupa, Markku**; Eckerman, Christer; **Kangas, Lauri**; Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni (Hormos Nutraceutical Oy Ltd., Finland). PCT Int. Appl. WO 2000059946 A1 20001012, 43 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-FI181 20000309. PRIORITY: US 1999-281094 19990330.

AB This invention relates to methods for prevention of cancers, certain non-cancer, hormone dependent diseases and/or cardiovascular diseases in a person, based on administering of hydroxymatairesinol to said person. The invention also concerns a method for increasing the level of **enterolactone** or another metabolite of hydroxymatairesinol in a person's serum thereby causing prevention of a cancer or a certain non-cancer, hormone dependent disease in a person, based on administering of hydroxymatairesinol to said person. Furthermore, this invention relates to pharmaceutical prepns., food additives and food products comprising hydroxymatairesinol.

L26 ANSWER 5 OF 5 MEDLINE DUPLICATE 2
2001103469 Document Number: 20348508. PubMed ID: 10890032. Hydroxymatairesinol, a novel **enterolactone** precursor with antitumor properties from coniferous tree (Picea abies). Saarinen N M; Warri A; Makela S I; Eckerman C; Reunanen M; **Ahotupa M**; Salmi S M; Franke A A; **Kangas L**; Santti R. (Department of Anatomy, University of Turku, Finland.) NUTRITION AND CANCER, (2000) 36 (2) 207-16. Journal code: 7905040. ISSN: 0163-5581. Pub. country: United States. Language: English.

AB The potential for the extraction of the plant lignan hydroxymatairesinol (HMR) in large scale from Norway spruce (Picea abies) has given us the opportunity to study the metabolism and biological actions of HMR in animals. HMR, the most abundant single component of spruce lignans, was metabolized to **enterolactone** (ENL) as the major metabolite in rats after oral administration. The amounts of urinary ENL increased with the dose of HMR (from 3 to 50 mg/kg), and only minor amounts of unmetabolized HMR isomers and other lignans were found in urine. HMR (15 mg/kg body wt po) given for 51 days decreased the number of growing tumors and increased the proportion of regressing and stabilized tumors in the rat dimethylbenz[a]anthracene-induced mammary tumor model. HMR (50 mg/kg body wt) did not exert estrogenic or antiestrogenic activity in the uterine growth test in immature rats. HMR also showed no antiandrogenic

responses in the growth of accessory sex glands in adult male rats. Neither ENL nor enterodiol showed estrogenic or antiestrogenic activity via a classical alpha- or beta-type estrogen receptor-mediated pathway in vitro at < 1.0 microM. HMR was an effective antioxidant in vitro.

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L27 315151 NEUTROPHIL

=> s l27 and macrophage
L28 50003 L27 AND MACROPHAGE

=> s l28 and oxidative burst
L29 518 L28 AND OXIDATIVE BURST

=> s l29 and inhibitor
L30 68 L29 AND INHIBITOR

=> s l30 and lignan
L31 0 L30 AND LIGNAN

=> s l30 adn hydroxymatairesinol
MISSING OPERATOR L30 ADN
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nested terms that are not separated by a logical operator.

=> s l30 and hydroxymatairesinol
L32 0 L30 AND HYDROXYMATAIRESINOL

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PROCESSING COMPLETED FOR L30
L33 38 DUP REMOVE L30 (30 DUPLICATES REMOVED)

=> d l33 1-38 cbib abs

L33 ANSWER 1 OF 38 MEDLINE
2002436220 Document Number: 22181529. PubMed ID: 12193733. Activation of peroxisome proliferator-activated receptor gamma by nitric oxide in monocytes/**macrophages** down-regulates p47phox and attenuates the respiratory burst. Von Knethen Andreas; Brune Bernhard. (Institute of Cell Biology, University of Kaiserslautern, Germany.) JOURNAL OF IMMUNOLOGY, (2002 Sep 1) 169 (5) 2619-26. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB NO appears as an important determinant in auto and paracrine **macrophage** function. We hypothesized that NO switches monocyte/**macrophage** function from a pro- to an anti-inflammatory phenotype by activating anti-inflammatory properties of the peroxisome proliferator-activated receptor (PPAR)gamma. NO-releasing compounds (100 micro M S-nitrosoglutathione or 50 micro M spermine-NONOate) as well as inducible NO synthase induction provoked activation of PPARgamma. This was proven by EMSAs, with the notion that supershift analysis pointed to the involvement of PPARgamma. PCR analysis ruled out induction of PPARgamma mRNA as a result of NO supplementation. Reporter assays, with a construct containing a triple PPAR response element in front of a thymidine kinase minimal promoter driving the luciferase gene, were positive in response to NO delivery. DNA binding capacity as well as the transactivating capability of PPARgamma were attenuated by addition of the antioxidant N-acetyl-cysteine or in the presence of the NO scavenger 2-phenyl-4,4,5,6-tetramethyl-imidazoline-1-oxyl 3-oxide. Having established that NO but not lipophilic cyclic GMP analogs activated PPARgamma, we verified potential anti-inflammatory consequences. The **oxidative burst** of **macrophages**, evoked by

phorbol ester, was attenuated in association with NO-elicited PPARgamma activation. A cause-effect relationship was demonstrated when PPAR response element decoy oligonucleotides, supplied in front of NO delivery, allowed to regain an oxidative response. PPARgamma-mediated down-regulation of p47 phagocyte oxidase, a component of the NAD(P)H oxidase system, was identified as one molecular mechanism causing inhibition of superoxide radical formation. We conclude that NO participates in controlling the pro- vs anti-inflammatory phenotype of **macrophages** by modulating PPARgamma.

L33 ANSWER 2 OF 38 MEDLINE
2002201824 Document Number: 21932259. PubMed ID: 11934805.
Pharmacological profile of PKF242-484 and PKF241-466, novel dual **inhibitors** of TNF-alpha converting enzyme and matrix metalloproteinases, in models of airway inflammation. Trifilieff Alexandre; Walker Christoph; Keller Thomas; Kottirsch Georg; Neumann Ulf. (Novartis Respiratory Research Centre, Horsham, East Sussex.. alexandre.trifilieff@pharma.novartis.com) . BRITISH JOURNAL OF PHARMACOLOGY, (2002 Apr) 135 (7) 1655-64. Journal code: 7502536. ISSN: 0007-1188. Pub. country: England: United Kingdom. Language: English.
AB 1. TNF-alpha converting enzyme (TACE) and matrix metalloproteinases (MMPs) are believed to play a role in various airway inflammatory disorders. Therefore we have tested the effect of two new **inhibitors** of TACE/MMPs (PKF242-484, PKF241-466) in models of airway inflammation. 2. PKF242-484 and PKF241-466 inhibited purified MMP-1, -2, -3, -9, -13 and rat collagenase at low nanomolar range. Both compounds inhibited the TNF-alpha release from activated human peripheral blood mononuclear cells with IC(50) values of 56+/-28 and 141+/-100 nM, respectively and had no significant effect on the activation of other human leukocytes, as neither **neutrophils** and eosinophils **oxidative burst** nor proliferation or cytokines production by T cells were inhibited in vitro. 3. PKF242-484 and PKF241-466 had beneficial effects in two different murine models of acute lung inflammation in vivo. The influx of **neutrophils** and lymphocytes into the airways was reduced 3 and 24 h after intranasal LPS challenge. This was accompanied by reduced levels of myeloperoxidase and elastase activities in the bronchoalveolar lavage. Furthermore, a complete inhibition of TNF-alpha release into the airways was observed. In addition, PKF242-484 effectively reduced the influx of **neutrophils**, eosinophils and lymphocytes in a model of acute allergic lung inflammation. 4. PKF242-484 and PKF241-466 are two novel and potent dual **inhibitors** of TACE and MMPs, which show activity in in vivo models of lung inflammation. Such compounds could have beneficial effects in airway inflammatory conditions such as asthma and chronic obstructive pulmonary disease.

L33 ANSWER 3 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
2002:297601 The Genuine Article (R) Number: 536YV. Pharmacological profile of a novel phosphodiesterase 4 **inhibitor**, 4-(8-benzo[1,2,5]oxadiazol-5-yl-[1,7]naphthyridin-6-yl)-benzoic acid (NVP-ABE171), a 1,7-naphthyridine derivative, with anti-inflammatory activities. Trifilieff A (Reprint); Wyss D; Walker C; Mazzoni L; Hersperger R. Novartis Horsham Resp Ctr, Wimblehurst Rd, Horsham RH12 5AB, W Sussex, England (Reprint); Novartis Horsham Resp Ctr, Horsham RH12 5AB, W Sussex, England; Novartis Pharma AG, Basel, Switzerland. JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS (APR 2002) Vol. 301, No. 1, pp. 241-248. Publisher: AMER SOC PHARMACOLOGY EXPERIMENTAL THERAPEUTICS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA. ISSN: 0022-3565. Pub. country: England; Switzerland. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB We investigated the pharmacology of a new class of phosphodiesterase 4 (PDE4) **inhibitor**, 6,8-disubstituted 1,7-naphthyridines, by using

4-(8-benzo[1,2,5] oxadiazol-5-yl-[1,7] naphthyridin- 6-yl)-benzoic acid (NVP-ABE171) as a representative compound and compared its potency with the most advanced PDE4 **inhibitor**, undergoing clinical trials, Ariflo [cis-4-cyano-4(3- cyclopentyloxy-4-methoxyphenyl-r-1-cyclohexanecarboxylic acid)]. NVP-ABE171 inhibited the activity of phosphodiesterase 4A, 4B, 4C, and 4D with respective IC50 values of 602, 34, 1230, and 1.5 nM. Ariflo was about 40 times less potent. In human cells, NVP-ABE171 inhibited the eosinophil and **neutrophil oxidative burst**, the release of cytokines by T cells, and the tumor necrosis factor-alpha release from monocytes, in the nanomolar range. Ariflo presented a similar inhibition profile but was 7 to 50 times less potent. In BALB/c mice challenged with lipopolysaccharide, NVP-ABE171 inhibited the airway **neutrophil** influx and activation with an ED50 in the range of 3 mg/kg. Ariflo was inactive up to a dose of 10 mg/kg. In ovalbumin sensitized Brown Norway rats, NVP-ABE171 inhibited the lipopolysaccharide-induced airway **neutrophil** influx and activation (ED50 of 0.2 mg/kg) and the ovalbumin-induced airway eosinophil influx and activation (ED50 of 0.1 mg/kg). Ariflo was about 100 times less potent in both models. In the ovalbumin model, NVP-ABE171 had a duration of action of more than 24 h. NVP-ABE171 is a novel PDE4 **inhibitor** that shows activity both in vitro on human inflammatory cells and in vivo in animal models of lung inflammation. This compound class may have potential for the treatment of airway inflammatory conditions such as asthma and chronic obstructive pulmonary diseases.

L33 ANSWER 4 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI

2002:540086 The Genuine Article (R) Number: 565WM. Low-density lipoprotein modification by normal, myeloperoxidase-deficient and NADPH oxidase-deficient granulocytes and the impact of redox active transition metal ions. Gerber C E; Bruchelt G; Ledinski G; Greilberger J; Niethammer D; Jurgens G (Reprint). Karl Franzens Univ Graz, Inst Med Chem, Harrachgasse 21, A-8010 Graz, Austria (Reprint); Karl Franzens Univ Graz, Inst Med Chem, A-8010 Graz, Austria; Karl Franzens Univ Graz, Pregl Lab, A-8010 Graz, Austria; Univ Tubingen, Childrens Hosp, Dept Hematol & Oncol, Tubingen, Germany. REDOX REPORT (SEP-OCT 2002) Vol. 7, No. 2, pp. 111-119. Publisher: W S MANEY & SONS LTD. HUDSON RD, LEEDS LS9 7DL, ENGLAND. ISSN: 1351-0002. Pub. country: Austria; Germany. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB The modification of low-density lipoprotein (LDL) by normal, myeloperoxidase (MPO)-deficient and NADPH oxidase-deficient granulocytes was investigated using the monoclonal antibody (mAb) OB/04, which was originally generated against copper-oxidized LDL. Incubation of LDL with normal granulocytes increased the reactivity of LDL with mAb OB/04. These effects were even more pronounced using MPO-deficient granulocytes. **Inhibitors** of oxidative reactions (the NADPH oxidase **inhibitor** diphenyleneiodonium chloride [DPI], catalase, superoxide dismutase [SOD]) did not significantly reduce LDL oxidation by normal granulocytes. Furthermore, granulocytes of a patient with NADPH oxidase deficiency were almost equally effective as normal granulocytes, indicating that **oxidative burst**-derived reactive oxygen species are of only minor importance in the generation of mAb OB/04-detectable new epitopes on LDL in vitro. In contrast, incubation of LDL with iron and copper prior to and during incubation with normal granulocytes markedly enhanced the generation of OB/04-detectable epitopes. It is supposed that, besides superoxide (in normal and MPO-deficient granulocytes) or instead of superoxide (in NADPH oxidase-deficient granulocytes), lytic enzymes released by activated granulocytes may enhance the availability of transition metals for oxidation of LDL. Our results support the concept that transition-metal-dependent pathways of LDL oxidation in combination with degranulation products of granulocytes are important.

L33 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2003 ACS
2001:833655 Document No. 135:356773 Diagnosis, treatment and prevention of steroid hormone-responsive cancers. Sirbasku, David A. (USA). PCT Int. Appl. WO 2001086307 A2 20011115, 332 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US15171 20010510. PRIORITY: US 2000-PV203314 20000510; US 2000-PV208348 20000531; US 2000-PV208111 20000531; US 2000-PV229071 20000830; US 2000-PV231273 20000908.

AB The author discloses culture media and methods that provide for assessment of the steroid hormone responsiveness of tumors of the breast and prostate, as well as other glandular/mucus epithelial tissues. In one example using the characterized culture system, the author demonstrates that estrogen-reversible inhibition of breast tumor cell proliferation is mediated by polyclonal IgA and IgM. The inhibition by these secretory Igs was shown to be dependent on the polymeric Ig receptor.

L33 ANSWER 6 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
2001:765438 The Genuine Article (R) Number: 474LU. 1
alpha,25-dihydroxyvitamin D-3-induced monocyte antimycobacterial activity is regulated by phosphatidylinositol 3-kinase and mediated by the NADPH-dependent phagocyte oxidase. Sly L M; Lopez M; Nauseef W M; Reiner N E (Reprint). Univ British Columbia, Div Infect Dis, Rm 452D, 2733 Heather St, Vancouver, BC V5Z 3J5, Canada (Reprint); Univ British Columbia, Dept Med, Div Infect Dis, Fac Med, Vancouver Hosp & Hlth Sci Ctr, Res Inst, Vancouver, BC V5Z 3J5, Canada; Univ British Columbia, Dept Med, Div Infect Dis, Fac Surg, Vancouver Hosp & Hlth Sci Ctr, Res Inst, Vancouver, BC V5Z 3J5, Canada; Univ British Columbia, Dept Microbiol & Immunol, Fac Surg, Vancouver Hosp & Hlth Sci Ctr, Res Inst, Vancouver, BC V5Z 3J5, Canada; Univ British Columbia, Dept Microbiol & Immunol, Fac Med, Vancouver Hosp & Hlth Sci Ctr, Res Inst, Vancouver, BC V5Z 3J5, Canada; Univ Iowa, Dept Med, Iowa City, IA 52246 USA; Vet Affairs Med Ctr, Iowa City, IA 52246 USA; Univ Iowa, Inflammat Program, Iowa City, IA 52246 USA. JOURNAL OF BIOLOGICAL CHEMISTRY (21 SEP 2001) Vol. 276, No. 38, pp. 35482-35493. Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA. ISSN: 0021-9258. Pub. country: Canada; USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We investigated the basis for the induction of monocyte antimycobacterial activity by 1 alpha ,25-dihydroxyvitamin D-3 (D-3). As expected, incubation of Mycobacterium tuberculosis-infected THP-1 cells or human peripheral blood, monocyte-derived **macrophages** with hormone resulted in the induction of antimycobacterial activity. This effect was significantly abrogated by pretreatment of cells with either of the phosphatidylinositol 3-kinase (PI 3-K) **inhibitors**, wortmannin or LY294002, or with antisense oligonueleotides to the p110 subunit of PI 3-K alpha. Cells infected with M. tuberculosis alone or incu- bated with D-3 alone produced little or undetectable amounts of superoxide anion (O . (-)(2)). In contrast, exposure of M. tuberculosis-infected cells to D-3 led to significant production of O . (-)(2) and this response was eliminated by either wortmannin, LY294002, or p110 antisense oligonucleotides. As was observed for PI 3-K inactivation, the reactive oxygen intermediate scavenger, 4-hydroxy-TEMPO, and degradative enzymes, polyethylene glycol coupled to either superoxide dismutase or catalase, also abrogated D-3-induced antimycobacterial activity. Superoxide production by THP-1 cells in response to D3 required

prior infection with live Al. tuberculosis, since exposure of cells to either killed M. tuberculosis or latex beads did not prime for an **oxidative burst** in response to subsequent hormone treatment. Consistent with these findings, redistribution of the cytosolic oxidase components p47(phox) and p67(phox) to the membrane fraction was observed in cells incubated with live M. tuberculosis and D-3 but not in response to combined treatment with heat-killed M. tuberculosis followed by D-3. Redistribution of p47(phox) and p67(phox) to the membrane fraction in response to live M. tuberculosis and D-3 was also abrogated under conditions where PI 3-K was inactivated. Taken together, these results indicate that D-3-induced, human monocyte antimycobacterial activity is regulated by PI 3-K and mediated by the NADPH-dependent phagocyte oxidase.

L33 ANSWER 7 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 1
2001134789 EMBASE Intracellular pool of IL-10 receptors in specific granules of human **neutrophils**: Differential mobilization by proinflammatory mediators. Elbim C.; Reglier H.; Fay M.; Delarche C.; Andrieu V.; El Benna J.; Gougerot-Pocidalo M.-A.. Dr. M.-A. Gougerot-Pocidalo, Lab. d'Immunologie et d'Hematologie, Ctr. Hospitalier Univ. Xavier Bichat, 46 rue Henri Huchard, 75877 Pads Cedex 18, France. pocidalo@bichat.inserm.fr. Journal of Immunology 166/8 (5201-5207) 15 Apr 2001.
Refs: 49.
ISSN: 0022-1767. CODEN: JOIMA3. Pub. Country: United States. Language: English. Summary Language: English.
AB IL-10 has a wide range of effects tending to control inflammatory responses. We used flow cytometry to study IL-10 binding at the polymorphonuclear **neutrophil** (PMN) surface and its modulation by various proinflammatory agents. Little IL-10 bound to the surface of resting PMN. However, binding was strongly increased after stimulation with LPS and proinflammatory cytokines such as TNF and GM-CSF. IL-1 and IL-8 did not significantly modify IL-10 binding. Cycloheximide had no effect on TNF-induced IL-10 binding, strongly suggesting the release of a pre-existing pool of IL-10R rather than de novo receptor synthesis by PMN. This was confirmed by the inhibitory effect of pentoxifylline, an **inhibitor** of degranulation. The existence of an intracellular pool of IL-10R was shown by flow cytometry, immunocytochemical staining, and Western blotting with several anti-human IL-10R Abs. In subcellular fractions of resting PMN, IL-10R was mainly located in the specific granule fraction, and was absent from azurophil granules and cytosol. We also tested the mobilization of specific granules by measuring the release of lactoferrin, their reference marker. The differential effects of the proinflammatory agents on IL-10 binding matched their effects on lactoferrin release and may therefore be related to differential mobilization of specific granules by these agents. Furthermore, the kinetics of TNF-induced up-regulation of IL-10 binding to PMN ran parallel to the kinetics of the inhibitory effect of IL-10 on the **oxidative burst**, suggesting a key role of IL-10R mobilization from specific granules to the membranes in optimal regulation of inflammatory responses.

L33 ANSWER 8 OF 38 MEDLINE
2001200851 Document Number: 21185311. PubMed ID: 11287316.
Mac-1-dependent tyrosine phosphorylation during **neutrophil** adhesion. Takami M; Herrera R; Petruzzelli L. (Department of Internal Medicine, University of Michigan Medical Center and Department of Veterans Affairs Medical Center, Ann Arbor 48109, USA.) AMERICAN JOURNAL OF PHYSIOLOGY. CELL PHYSIOLOGY, (2001 May) 280 (5) C1045-56. Journal code: 100901225. ISSN: 0363-6143. Pub. country: United States. Language: English.
AB Activated **neutrophils** display an array of physiological responses, including initiation of the **oxidative burst**, phagocytosis, and cell migration, that are associated with cellular

adhesion. Under conditions that lead to cellular adhesion, we observed rapid tyrosine phosphorylation of an intracellular protein with an approximate relative molecular mass of 92 kDa (p92). Phosphorylation of p92 was inducible when Mac-1 was activated by phorbol 12-myristate 13-acetate, the beta(2)-specific activating antibody CBR LFA-1/2, or interleukin-8 (77 amino acids). In addition, tyrosine phosphorylation of p92 was dependent on engagement of Mac-1 with ligand. Several observations suggest that this event may be an important step in the signaling pathway initiated by Mac-1 binding. p92 phosphorylation was specifically blocked with antibodies to CD11b, the alpha-subunit of Mac-1, and was rapidly reversible on disengagement of the integrin ligand interaction. Integrin-stimulated phosphorylation of p92 created binding sites that were recognized in vitro by the SH2 domains of c-CrkII and Src. Our observations suggest that **neutrophil** adhesion mediated through the binding of the beta(2)-integrin Mac-1 initiates a signaling cascade that involves the activation of protein tyrosine kinases and leads to the regulation of protein-protein interactions via SH2 domains, a key process shared with growth factor signaling pathways.

L33 ANSWER 9 OF 38 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
2002:129516 Document No.: PREV200200129516. Interaction between SHPS-1 and CD47 mediates the adhesion of human B lymphocytes to non-activated endothelial cells. Yoshida, Hitoshi (1); Tomiyama, Yoshiaki (1); Oritani, Kenji (1); Honma, Nakayuki; Matsuzawa, Yuji (1). (1) Internal Medicine and Molecular Science, Graduate School of Medicine, Osaka University, Suita, Osaka Japan. Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 21a. http://www.bloodjournal.org/. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001 ISSN: 0006-4971. Language: English.

AB CD47, also known as integrin-associated protein, is an ubiquitously exressed 50-kd cell surface glycoprotein with an extracellular immunoglobulin domain and 5 putative transmembrane domains. It physically and functionally associates with beta 3 integrins and modulates a variety of cell functions including cell activation, adhesion, migration, and phagocytosis. Treatment of leukocytes with anti-CD47 monoclonal antibodies (mAbs) modulates beta3 integrin-mediated ligand binding, activation, **oxidative burst**, and Fc receptor-mediated phagocytosis. **Neutrophils** require CD47 to migrate across the endothelial and colonic epithelial cells after firm adhesion. We have recently demonstrated that soluble form of an anti-CD47 mAb B6H12 induces polarization in these B cell lines via the activation of Cdc42, a member of Rho family small GTPase in an integrin-independent manner. These findings suggest that CD47 itself may transduce polarization signals into B lymphocytes. Because these studies have been conducted by using some ligand-mimic anti-CD47 mAbs, the roles of interactions between CD47 and its ligands thrombospondin (TSP) and SHPS-1, still remain elusive. Employing a fusion protein consisted of the extracellular region of SHPS-1 and the Fc portion of human immunoglobulin (SHPS-1-Ig), we investigated the effects of SHPS-1 as a ligand for CD47 on B lymphocytes. Although SHPS-1-Ig binding to human B cell lines was solely mediated via CD47, their binding capacity for soluble and immobilized SHPS-1-Ig varied among cell lines irrespective of the similar expression levels of CD47, suggesting that distinctive affinity/avidity states exist during B cell maturation. Nalm6 cell line and tonsilar B lymphocytes adhered to immobilized SHPS-1-Ig and showed polarization-like morphology. These effects of SHPS-1-Ig were blocked by anti-CD47 mAbs (B6H12 and SE5A5) but not 4N1K, a functional peptide of thrombospondin (TSP). Wortmannin, a phosphatidyl inotitol-3 kinase **inhibitor**, but not pertussis toxin significantly inhibited the polarization induced by the immobilized SHPS-1-Ig. Thus, SHPS-1 acts as an adhesive substrate via CD47 in human B lymphocyte, and the SHPS-1 binding site in CD47 is probably different from the TSP binding site. Immunohistochemical analyses indicated that SHPS-1

is expressed on high endothelial venule as well as **macrophages** in human tonsils. Human umbilical vein endothelial cells (HUVECs) also express SHPS-1 in the absence of any stimuli, and the adhesion of tonsilar B lymphocytes to non-activated HUVECs was significantly inhibited By SE5A5, indicating that SHPS 1/CD47 interaction is involved in the adhesion. Our findings suggest that SHPS-1/CD47 interaction may contribute to the recruitment of B lymphocytes via endothelial cells under steady state conditions.

L33 ANSWER 10 OF 38 MEDLINE DUPLICATE 2
2000514153 Document Number: 20523257. PubMed ID: 11073105. Monoclonal Lym-1 antibody-targeted lysis of B lymphoma cells by **neutrophils**. Evidence for two mechanisms of FcgammaRII-dependent cytolysis. Ottonello L; Epstein A L; Mancini M; Amelotti M; Dapino P; Dallegri F. (Department of Internal Medicine, University of Genova Medical School, Italy.) *JOURNAL OF LEUKOCYTE BIOLOGY*, (2000 Nov) 68 (5) 662-8. Journal code: 8405628. ISSN: 0741-5400. Pub. country: United States. Language: English.

AB Human **neutrophils** incubated with the anti-HLA-DR mAb Lym-1, plus PMA, induced significant cytolysis of B lymphoma cells compared with Lym-1 and PMA alone. The effect of PMA was independent of the ability of the compound to stimulate **neutrophil**-respiratory burst. In fact, first, **neutrophils** from a patient with chronic granulomatous disease were cytolytically effective in spite of their inability to produce oxidants. Second, various kinase **inhibitors** exerted different effects on the PMA-stimulated cytolytic system and **neutrophil-oxidative burst**. Previous studies have shown the involvement of the FcgammaRII, CD11b-CD18 integrins, and CD66b glycoproteins in the Lym-1 mAb-dependent cytolysis by GM-CSF-stimulated **neutrophils**. The present PMA-stimulated system was inhibited by the anti-FcgammaRII mAb IV.3, the anti-CD18 mAb MEM 48, and the anti-CD11b mAb 2LPM19c but not by the anti-CD66b mAb 80H3 and N-acetyl-D-glucosamine. Furthermore, the PMA- and GM-CSF-stimulated cytolysis was insensitive and sensitive to inhibition by pertussis toxin, respectively. Thus, the use of PMA and GMCSF as **neutrophil** stimulants uncovers the existence of distinct mechanisms of Lym-1 mAb-mediated cytolysis.

L33 ANSWER 11 OF 38 MEDLINE
2000487716 Document Number: 20489674. PubMed ID: 11037974. Escherichia coli cytotoxic necrotizing factor-1 (CNF-1) increases the adherence to epithelia and the **oxidative burst** of human polymorphonuclear leukocytes but decreases bacteria phagocytosis. Hofman P; Le Negrate G; Mograbi B; Hofman V; Brest P; Alliana-Schmid A; Flatau G; Boquet P; Rossi B. (Laboratoire d'Anatomie-Pathologique, INSERM U364, Nice, France.. hofman@unice.fr) . JOURNAL OF LEUKOCYTE BIOLOGY, (2000 Oct) 68 (4) 522-8. Journal code: 8405628. ISSN: 0741-5400. Pub. country: United States. Language: English.

AB Recruitment of polymorphonuclear leukocytes (PMNL) is a hallmark of both urinary and digestive infections caused by Escherichia coli. Cytotoxic necrotizing factor 1 (CNF-1) is a toxin produced by uropathogenic E. coli strains that mediates its effects via the activation of small GTP-binding proteins. However, the role and the consequences of CNF-1 on PMNL physiology remain largely unknown. In this study, we provide evidence that CNF-1 dramatically affects the PMNL cytoskeleton architecture by inducing an increased content of F-actin. Furthermore, we demonstrate that CNF-1 increases functional features of PMNL, such as superoxide generation and adherence on epithelial T84 monolayers, but significantly decreases their phagocytic function. Our results suggest that CNF-1 may behave as a virulence factor in urinary or digestive infection by stimulating PMNL cytotoxicity as a result of its enhancing effect on their adherence to epithelial cells as well as the production of radical oxygen products. Moreover, the decreased phagocytosis of PMNL induced by CNF-1

likely facilitates growth of bacteria. In these conditions, CNF-1 would intervene in the initiation and in the perpetuation of the inflammatory process.

L33 ANSWER 12 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
1999:919097 The Genuine Article (R) Number: 258MT. 15-deoxy-Delta(12,14)-prostaglandin J(2) inhibits the beta(2) integrin-dependent **oxidative burst**: Involvement of a mechanism distinct from peroxisome proliferator-activated receptor gamma ligation. Vaidya S; Somers E P; Wright S D; Detmers P A; Bansal V S (Reprint). MERCK RES LABS, 126 E LINCOLN AVE, RY80W-250, RAHWAY, NJ 07065 (Reprint); MERCK RES LABS, RAHWAY, NJ 07065. JOURNAL OF IMMUNOLOGY (1 DEC 1999) Vol. 163, No. 11, pp. 6187-6192. Publisher: AMER ASSOC IMMUNOLOGISTS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0022-1767. Pub. country: USA. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB 15-Deoxy-Delta(12,14)-PGJ(2) (dPGJ(2)) is a bioactive metabolite of the J(2) series that has been identified as a ligand for peroxisome proliferator-activated receptor gamma (PPAR gamma) and has received attention for its potential antiinflammatory effects. Because **neutrophils** express cell-surface receptors for PGs, the effect of dPGJ(2) was tested on an inflammatory response that should not require PPAR gamma, the **oxidative burst** made by adherent human **neutrophils**. dPGJ(2) inhibited adhesion-dependent H2O2 production with an IC50 of 1.5 mu M when **neutrophils** were stimulated with TNF, N-formylnorleucyleucylphenylalanine, or LPS, Inhibition by dPGJ(2) occurred during the lag phase, before generation of peroxide, suggesting blockade of an early signaling step. Indeed, dPGJ(2) blocked adhesion of **neutrophils** to fibrinogen in response to TNF or LPS with an IC50 of 3-5 mu M dPGJ(2) was more potent at inhibiting the adhesion-dependent **oxidative burst** than several other PGs tested. Further, dPGJ(2) did not appear to act through either the DP receptor or receptors for PGE(2), PG receptors modulate cAMP levels, and the inhibition of adhesion and **oxidative burst** by dPGJ(2) was enhanced in the presence of 3-isobutyl-1-methylxanthine, a cAMP phosphodiesterase **inhibitor**. A potent PPAR gamma agonist (AD-5075) did not inhibit peroxide production or adhesion, nor did it change the IC50 for dPGJ(2) inhibition. These studies suggest that dPGJ(2) may interact with an unknown receptor on **neutrophils**, distinct from PPAR gamma, to modulate the production of reactive oxygen intermediates.

L33 ANSWER 13 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
1999:476528 The Genuine Article (R) Number: 206LY. Substance P primes the formation of hydrogen peroxide and nitric oxide in human **neutrophils**. SternerKock A; Braun R K; vanderVliet A; Schrenzel M D; McDonald R J; Kabbur M B; Vulliet P R; Hyde D M (Reprint). UNIV CALIF DAVIS, SCH VET MED, DEPT ANAT PHYSIOL & CELL BIOL, DAVIS, CA 95616 (Reprint); UNIV CALIF DAVIS, SCH VET MED, DEPT ANAT PHYSIOL & CELL BIOL, DAVIS, CA 95616; UNIV CALIF DAVIS, SCH MED, DEPT INTERNAL MED, DAVIS, CA 95616; UNIV CALIF DAVIS, SCH VET MED, DEPT PATHOL MICROBIOL & IMMUNOL, DAVIS, CA 95616; UNIV CALIF DAVIS, SCH MED, DEPT PEDIAT, DAVIS, CA 95616; UNIV CALIF DAVIS, SCH VET MED, DEPT MOL BIOSCI, DAVIS, CA 95616. JOURNAL OF LEUKOCYTE BIOLOGY (JUN 1999) Vol. 65, No. 6, pp. 834-840. Publisher: FEDERATION AMER SOC EXP BIOL. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 . ISSN: 0741-5400. Pub. country: USA. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Substance P (SP), a neurotransmitter of the central and peripheral nervous system, has been implicated as a mediator of the pulmonary inflammatory response through its stimulatory effects on **neutrophils**. We investigated the role of SP in priming the production of reactive oxygen species by human **neutrophils** with the cytochrome c reduction assay and by flow cytometry using the intracellular oxidizable probe dichlorofluorescein. We also investigated

SP-induced formation of nitrite and nitrate as an index of nitric oxide (NO) production, Our results indicate that SP primes two distinct pathways with respect to the induction of reactive oxygen species in the human **neutrophil**: the production of superoxide anion and hydrogen peroxide by the calmodulin-dependent NADPH oxidase, and the generation of NO by a constitutive NO synthase. Preincubation of **neutrophils** with **inhibitors** of calmodulin and NO synthase diminished the oxidative response in an additive fashion, These results give insight into distinct signal transduction pathways in the SP-primed **neutrophil** with respect to the formation of superoxide anion, hydrogen peroxide, and NO.

L33 ANSWER 14 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI

1998:952528 The Genuine Article (R) Number: 146YY. A novel mechanism for bradykinin production at inflammatory sites - Diverse effects of a mixture of **neutrophil** elastase and mast cell tryptase versus tissue and plasma kallikreins on native and oxidized kininogens. Kozik A; Moore R B; Potempa J; Imamura T; RapalaKozik M; Travis J (Reprint). UNIV GEORGIA, DEPT BIOCHEM & MOL BIOL, ATHENS, GA 30602 (Reprint); UNIV GEORGIA, DEPT BIOCHEM & MOL BIOL, ATHENS, GA 30602; JAGIELLONIAN UNIV, INST MOL BIOL, PL-31120 KRAKOW, POLAND; KUMAMOTO UNIV, GRAD SCH MED SCI, DIV MOL PATHOL, KUMAMOTO 860, JAPAN. JOURNAL OF BIOLOGICAL CHEMISTRY (11 DEC 1998) Vol. 273, No. 50, pp. 33224-33229. Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0021-9258. Pub. country: USA; POLAND; JAPAN. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Coprocessing of kininogens by a mixture of human mast cell tryptase and **neutrophil** elastase was explored as a potential substitute for the kallikrein-dependent pathway for kinin generation during inflammation. Tryptase easily excised bradykinin from the synthetic heptadecapeptide, ISLMKRPPGFSPFRSSR, but was unable to produce significant amounts of kinin by proteolysis of kininogens. However, a mixture of tryptase and elastase released bradykinin from each protein with a yield comparable to that of human plasma kallikrein, Significantly, neither plasma nor tissue kallikrein was able to effectively process N-chlorosuccinimide-oxidized high molecular weight kininogen, an effect attributed to the oxidation of a methionine residue upstream from the N terminus of the kinin domain. In support of these results the model heptadecapetide, ISL(MO)KRPPGFSPFRSSR, was also resistant to hydrolysis by either kallikrein. In contrast, the release of bradykinin from oxidized peptide or protein substrates by the tryptase/elastase mixture was not altered. Because kininogen modification may occur at inflammatory sites, as a result of the **oxidative burst** of recruited **neutrophils** and **macrophages**, these results suggest an alternative pathway for kinin production and the necessity for the novel utilization of two specific proteinases known to be released from these cells during inflammatory episodes.

L33 ANSWER 15 OF 38 CAPLUS COPYRIGHT 2003 ACS

1998:373146 Document No. 129:26780 Ligation of CD31/PECAM-1 modulates the function of lymphocytes, monocytes, and **neutrophils**. Elias, Chester G., III.; Spellberg, Jason P.; Karan-Tamir, Barbara; Lin, Chi-Hwei; Wang, Yueh-Ju; McKenna, Patrick J.; Muller, William A.; Zukowski, Mark M.; Andrew, David P. (Department Inflammation, Amgen Boulder Inc., Boulder, USA). European Journal of Immunology, 28(6), 1948-1958 (English) 1998. CODEN: EJIMAF. ISSN: 0014-2980. Publisher: Wiley-VCH Verlag GmbH.

AB CD31 or platelet/endothelial cell adhesion mol. (PECAM-1) is a 130-kDa glycoprotein expressed on endothelial cells, granulocytes, a subset of lymphocytes, and platelets. The authors examd. the ability of 4 monoclonal antibodies (mAb) against different domains of CD31 to modulate the function of T lymphocytes, monocytes, and **neutrophils**. Engagement of CD31 on T lymphocytes results in co-stimulation of T

lymphocyte proliferation to suboptimal doses of anti-CD31 mAb. This proliferation is accompanied by secretion of numerous cytokines and chemokines, up-regulation of CD25, and an increase in cell size. Purifn. of T lymphocytes into CD45RO and CD45RA subsets showed that only naive CD45RA T lymphocytes are co-stimulated by anti-CD31 mAb. Further studies on **neutrophils** show that engagement of CD31 results in down-regulation of CD62L and up-regulation of CD11b/CD18 as well as **oxidative burst**, as assessed by superoxide release. Ligation of CD31 on monocytes results in TNF-.alpha. secretion, and studies with various cell signaling **inhibitors** indicate that Tyr kinases and cAMP-dependent kinases are involved in monocyte activation via CD31. Of the 4 mAb used in this study, only 2 activated human leukocytes. These mAb were PECAM-1.3 and hec7, which bind to domains 1 and 2 of CD31. The authors conclude that engagement of domains 1 and 2 of CD31 results in outside-in signaling in leukocytes.

L33 ANSWER 16 OF 38 MEDLINE DUPLICATE 3

1998211727 Document Number: 98211727. PubMed ID: 9552001. Importance of MEK in **neutrophil** microbicidal responsiveness. Downey G P; Butler J R; Tapper H; Fialkow L; Saltiel A R; Rubin B B; Grinstein S. (Toronto Hospital, and Department of Medicine, University of Toronto, Ontario, Canada.. gregory.downey@utoronto.ca) . JOURNAL OF IMMUNOLOGY, (1998 Jan 1) 160 (1) 434-43. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Exposure of **neutrophils** to inflammatory stimuli such as the chemoattractant FMLP leads to activation of responses including cell motility, the **oxidative burst**, and secretion of proteolytic enzymes. A signaling cascade involving sequential activation of Raf-1, mitogen-activated protein kinase (MEK), and extracellular signal regulated kinase (ERK) is also rapidly activated after agonist exposure. The temporal relationship between these events suggests that the kinases may be involved in triggering the effector functions, but direct evidence of a causal relationship is lacking. To assess the role of the MEK/ERK pathway in the activation of **neutrophil** responses, we studied the effects of PD098059, a potent and selective **inhibitor** of MEK. Preincubation of human **neutrophils** with 50 microM PD098059 almost completely (>90%) inhibited the FMLP-induced activation of MEK-1 and MEK-2, the isoforms expressed by **neutrophils**. This dose of PD098059 virtually abrogated chemoattractant-induced tyrosine phosphorylation and activation of ERK-1 and ERK-2, implying that MEKs are the predominant upstream activators of these mitogen-activated protein kinases. Pretreatment of **neutrophils** with the MEK antagonist inhibited the **oxidative burst** substantially and phagocytosis only moderately. In addition, PD098059 antagonized the delay of apoptosis induced by exposure to granulocyte-**macrophage** CSF. However, the effects of PD098059 were selective, as it failed to inhibit other responses, including chemoattractant-induced exocytosis of primary and secondary granules, polymerization of F-actin, chemotaxis, or activation of phospholipase A2. We conclude that MEK and ERK contribute to the activation of the **oxidative burst** and phagocytosis, and participate in cytokine regulation of apoptosis.

L33 ANSWER 17 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

1998249431 EMBASE Pharmacology of benzydamine. Quane P.A.; Graham G.G.; Ziegler J.B.. G.G. Graham, Sch. of Physiology and Pharmacology, University of NSW, Sydney, NSW 2052, Australia. Inflammopharmacology 6/2 (95-107) 1998.
Refs: 57.
ISSN: 0925-4692. CODEN: IAOAES. Pub. Country: Netherlands. Language: English. Summary Language: English.

AB Benzydamine is a topical anti-inflammatory drug which is widely available and used topically for the treatment of the mouth. It is also used as a

gel for application to inflamed joints. It has physicochemical properties and pharmacological activities which differ markedly from those of the aspirin-line nonsteroidal anti-inflammatory drugs. Benzydamine is a weak base unlike the aspirin-like drugs which are acids or metabolized to acids. A major contrast with the aspirin-like drugs is that benzydamine is a weak **inhibitor** of the synthesis of prostaglandins but it has several properties which may contribute to its anti-inflammatory activity. These properties include inhibition of the synthesis of the inflammatory cytokine, tumour necrosis factor-.alpha. (EC50, 25 .mu.mol/L). Inhibition of the **oxidative burst** of **neutrophils** occurs under some conditions at concentrations of 30 to 100 .mu.mol/L, concentrations which may be produced within oral tissues after local application. A further activity of benzydamine is a general activity known as membrane stabilization which is demonstrated by several actions including inhibition of granule release from **neutrophils** at concentrations ranging from 3 to 30 .mu.mol/L and stabilization of lysosomes. Lack of knowledge of the tissue concentrations of benzydamine limit the correlation between pharmacological activities in vitro and in vivo. The concentration of benzydamine in the mouthwash is 4 mmol/L but the concentrations in oral tissues have not been studied adequately. Limited data in the rat indicates that concentrations of benzydamine in oral tissues are approximately 100 .mu.mol/L.

L33 ANSWER 18 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI

97:394418 The Genuine Article (R) Number: WZ384. Inhibition of NADPH oxidase activation by 4-(2-aminoethyl)-benzenesulfonyl fluoride and related compounds. Diatchuk V; Lotan O; Koshkin V; Wikstroem P; Pick E (Reprint). TEL AVIV UNIV, SACKLER FAC MED, DEPT HUMAN MICROBIOL, IL-69978 TEL AVIV, ISRAEL (Reprint); TEL AVIV UNIV, SACKLER FAC MED, DEPT HUMAN MICROBIOL, IL-69978 TEL AVIV, ISRAEL; PENTAPHARM LTD, CH-4002 BASEL, SWITZERLAND. JOURNAL OF BIOLOGICAL CHEMISTRY (16 MAY 1997) Vol. 272, No. 20, pp. 13292-13301. Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0021-9258. Pub. country: ISRAEL; SWITZERLAND. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The elicitation of an **oxidative burst** in phagocytes rests on the assembly of a multicomponental complex (NADPH oxidase) consisting of a membrane-associated flavocytochrome (cytochrome b(559)), representing the redox element responsible for the NADPH-dependent reduction of oxygen to superoxide (O-2(radical anion)), two cytosolic components (p47(phox), p67(phox)), and the small GTPase Rac (1 or 2), We found that 4-(2-aminoethyl)-benzenesulfonyl fluoride (AEBSF), an irreversible serine protease **inhibitor**, prevented the elicitation of O-2(radical anion) production in intact **macrophages** and the amphiphile-dependent activation of NADPH oxidase in a cell free system, consisting of solubilized membrane or purified cytochrome b(559) combined with total cytosol or a mixture of recombinant p47(phox), p67(phox), and Rad. AEBSF acted at the activation step and did not interfere with the ensuing electron flour, It did not scavenge oxygen radicals and did not affect assay reagents, Five other serine protease **inhibitors** (three irreversible and two reversible) were found to lack an inhibitory effect on cell-free activation of NADPH oxidase, A structure-function study of AEBSF analogues demonstrated that the presence of a sulfonyl fluoride group was essential for inhibitory activity and that compounds containing an aminoalkylbenzene moiety were more active than amidinobenzene derivatives, Exposure of the membrane fraction or of purified cytochrome b(559), but not of cytosol or recombinant cytosolic components, to AEBSF, in the presence of a critical concentration of the activating amphiphile lithium dodecyl sulfate, resulted in a marked impairment of their ability to support cell-free NADPH oxidase activation upon complementation with untreated cytosol or cytosolic components, Kinetic analysis of the effect of varying the concentration of each of the

three cytosolic components on the inhibitory potency of AEBSF indicated that this was inversely related to the concentrations of p47(phox) and, to a lesser degree, p67(phox), AEBSF also prevented the amphiphile-elicited translocation of p47(phox) and p67(phox) to the membrane, These results are interpreted as indicating that AEBSF interferes with the binding of p47(phox) and/or p67(phox) to cytochrome b(559), probably by a direct effect on cytochrome b(559).

L33 ANSWER 19 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
97:690346 The Genuine Article (R) Number: XV690. Regulations of cytosolic free Ca2+ in cultured rat alveolar **macrophages** (NR8383). Zhang G H (Reprint); Helmke R J; Mork A C; Martinez J R. UNIV TEXAS, HLTH SCI CTR, DEPT PEDIAT, 7703 FLOYD CURL DR, SAN ANTONIO, TX 78284 (Reprint). JOURNAL OF LEUKOCYTE BIOLOGY (SEP 1997) Vol. 62, No. 3, pp. 341-348. Publisher: FEDERATION AMER SOC EXP BIOL. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998. ISSN: 0741-5400. Pub. country: USA. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Ca2+ mobilization in the rat alveolar **macrophage** cell line NR8383 was examined with the Ca2+-sensitive fluorescent probe Fura-2. ATP and norepinephrine elicited a 108 and 46% increase, respectively, in cytosolic free Ca2+ concentration ([Ca2+](i)). Acetylcholine, nicotine, isoproterenol, substance P, and vasoactive intestinal polypeptide did not alter [Ca2+](i). Inositol 1,4,5-trisphosphate (IP3) formation was also activated by ATP. The carbohydrate-rich cell wall preparation, zymosan, induced a gradual [Ca2+](i) increase only in the presence of external Ca2+, but did not activate IP3 formation. This increase was abolished by laminarin and by removal of extracellular Ca2+, suggesting that the [Ca2+](i) Increase was activated by B-glucan receptors and mediated by Ca2+ influx. This influx was significantly reduced by SKF96365, but not by nifedipine, omega-conotoxin GVIA, omega-agatoxin TVA, or flunarizine. These results suggest that release of intracellular Ca2+ in MR8383 cells is regulated by P-2-purinoceptors and that zymosan causes Ca2+ influx via a receptor-operated pathway.

L33 ANSWER 20 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
97:920114 The Genuine Article (R) Number: YK700. Silica induces changes in cytosolic free calcium, cytosolic pH, and plasma membrane potential in bovine alveolar **macrophages**. Tarnok A (Reprint); Schluter T; Berg I; Gercken G. UNIV HOSP, HEART CTR LEIPZIG GMBH, PEDIAT CARDIOL, RUSSENSTR 19, D-04289 LEIPZIG, GERMANY (Reprint); OTTO VON GUERICKE UNIV, DEPT MED, INST BIOCHEM, MAGDEBURG, GERMANY; UNIV HAMBURG, HOSP EPPENDORF, DEPT ENZYME CHEM, INST PHYSIOL CHEM, D-20246 HAMBURG, GERMANY; UNIV HAMBURG, INST BIOCHEM & FOOD CHEM, DEPT BIOCHEM & MOL BIOL, HAMBURG, GERMANY. ANALYTICAL CELLULAR PATHOLOGY (DEC 1997) Vol. 15, No. 2, pp. 61-72. Publisher: IOS PRESS. VAN DIEMENSTRAAT 94, 1013 CN AMSTERDAM, NETHERLANDS. ISSN: 0921-8912. Pub. country: GERMANY. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB The mineral-dust induced activation of pulmonary phagocytes is thought to be involved in the induction of severe lung diseases. The activation of bovine alveolar **macrophages** (BAM) by silica was investigated by flow cytometry. Shortterm incubation (<10 min) of BAM with silica gel and quartz dust particles induced increases in the cytosolic free calcium concentration ([Ca2+](i)), decreases in intracellular pH (pH(i)), and increases in plasma membrane potential (PMP). The extent of these changes was concentration dependent, related to the type of dust and was due to Ca2+ influx from the extracellular medium. An increase in [Ca2+](i) was inhibited, when extracellular Ca2+ was removed. Furthermore the calcium signal was quenched by Mn2+ and diminished by the calcium channel blocker verapamil. The protein kinase C specific **inhibitor** bisindolylmaleimide II (GF 109203 X) did not inhibit the silica-induced [Ca2+](i) rise. In contrast, silica-induced cytosolic acidification and depolarization were inhibited by GF 109203 X but not by removal of

extracellular calcium. Addition of TiO2 particles or heavy metal-containing dusts had no effect on any of the three parameters. Our data suggest the existence of silica-activated transmembrane ion exchange mechanisms in BAM, which might be involved in the specific cytotoxicity of silica by Ca2+-dependent and independent pathways.

L33 ANSWER 21 OF 38 CAPLUS COPYRIGHT 2003 ACS
1996:435327 Document No. 125:104605 U-73122: a potent **inhibitor** of human polymorphonuclear **neutrophil** adhesion on biological surfaces and adhesion-related effector functions. Smith, Robert J.; Justen, James M.; McNab, Alistair R.; Rosenbloom, Craig L.; Steele, Addison N.; Detmers, Patricia A.; Anderson, Donald C.; Manning, Anthony M. (Cell Biol. and Inflammation Res., Pharmacia & Upjohn, Inc., Kalamazoo, MI, USA). Journal of Pharmacology and Experimental Therapeutics, 278(1), 320-329 (English) 1996. CODEN: JPETAB. ISSN: 0022-3565. Publisher: Williams & Wilkins.
AB We have reported that U-73122 (1-[6-[[17.beta.-3-methoxyestra-1,3,5(10)-trien-17-yl]amino]hexyl]-1H-pyrrole-2,5-dione), an **inhibitor** of phospholipase C-dependent processes in human polymorphonuclear **neutrophils** (PMN) and platelets, potently suppresses the responsiveness of suspended PMN and platelets to receptor agonists. We demonstrate here that U-73122 caused a concn.-dependent (10-800 nM) inhibition of N-formyl-methionyl-leucyl-phenylalanine, tumor necrosis factor-.alpha. (TNF-.alpha.), interleukin-8 and phorbol myristate acetate (PMA)-triggered PMN adhesion on fibronectin, fetal bovine serum or keyhole limpet hemocyanin-coated microtiter plates. U-73122 also inhibited PMN adherence to and transmigration through TNF-.alpha.-activated endothelium (IC50 < 50 nM). Further, U-73122 suppressed interleukin-8, N-formyl-methionyl-leucyl-phenylalanine and PMA-stimulated up-regulation of the .beta.2-integrin, Mac-1 (CD11b/CD18), on the PMN surface (IC50 < 1.3 .mu.M), U-73122 also caused a time- (15-120 min) and concn.-dependent inhibition (IC50 = 25-100 nM) of the N-formyl-methionyl-leucyl-phenylalanine-, TNF.alpha.- and PMA-elicited adhesion-dependent **oxidative burst**, measured as hydrogen peroxide (H2O2) prodn., in PMN. The CD18-dependent extracellular release of lactoferrin from PMN activated with these stimuli was also suppressed by U-73122. U-73343 (1-[6-[[17.beta.-3-methoxyestra-1,3,5(10)-trien-17-yl]amino]hexyl]-2,5-pyrrolidinedione), a close analog of U-73122, did not affect PMN responsiveness.

L33 ANSWER 22 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
95:653309 The Genuine Article (R) Number: RV167. EFFECT OF CAPSAICIN ON PHOSPHOLIPASE A(2) ACTIVITY AND SUPEROXIDE GENERATION IN **MACROPHAGES**. SAVITHA G; SALIMATH B P (Reprint). MANASAGANGOTRI UNIV MYSORE, DEPT BIOCHEM, MYSORE 570006, KARNATAKA, INDIA (Reprint); MANASAGANGOTRI UNIV MYSORE, DEPT BIOCHEM, MYSORE 570006, KARNATAKA, INDIA. NUTRITION RESEARCH (OCT 1995) Vol. 15, No. 10, pp. 1417-1427. ISSN: 0271-5317. Pub. country: INDIA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The mechanism of inhibition of Ca2+ - triggered phospholipase A(2) (PLA(2)) activity and respiratory burst in **macrophages** by shown that capsaicin inhibits calcium-ionophore stimulated pro-inflammatory responses in **macrophages** such as generation of superoxide anion, PLA(2) activity (IC50 = 20 uM) and membrane liquid peroxidation (IC50 = 10 uM). Both capsaicin and PLA(2) and dose dependent manner. Arachidonic acid, linoleic acid and SDS restored capsaicin inhibited respiratory burst. Capsaicin and known PLA(2) **inhibitors**, dexamethasone and indomethacin, inhibited Ca2+-dependent PLA(2) activity in vitro from **macrophages**. Inhibition of PLA(2) activity by capsaicin is independent of Ca2+ and substrate concentration. Fluorescence studies studies suggest that capsaicin interacts directly with partially purified **macrophage** PLA(2). Finally, the antioxidant property of capsaicin

was comparable to that of butylated hydroxy toludine (BHT). Taken together these results show that capsaicin an antiinflammatory agent with potential clinical application.

L33 ANSWER 23 OF 38 MEDLINE DUPLICATE 4
96288303 Document Number: 96288303. PubMed ID: 8707444. The specific type IV phosphodiesterase **inhibitor** rolipram combined with adenosine reduces tumor necrosis factor-alpha-primed **neutrophil** oxidative activity. Sullivan G W; Carper H T; Mandell G L. (Department of Medicine, University of Virginia, Charlottesville 22908, USA.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (1995 Oct) 17 (10) 793-803. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Monocytes and **macrophages** produce tumor necrosis factor-alpha (TNF alpha) in response to microbial products including endotoxin. TNF alpha is a potent primer of **neutrophil** (PMN) oxidative activity. Certain xanthine phosphodiesterase (PDE) **inhibitors** such as pentoxifylline have been shown to inhibit stimulated oxidative activity in PMN. In the present study, the non-xanthine PDE type IV **inhibitor** rolipram (4-[3'-cyclopentyloxy-4'-methoxyphenyl]-2-pyrrolidone) alone and in combination with adenosine is examined as a potential modulator of TNF alpha-primed PMN oxidative activity. Attainable in vivo concentrations of rolipram and physiological concentrations of adenosine alone and together synergistically decreased rhTNF alpha-primed suspended PMN oxidative activity stimulated by the chemoattractant f-met-leu-phe. The rolipram effect was reversible by washing, and rolipram had a comparable effect if added before or after priming, indicating that its effect was on the primed response rather than on priming per se. In addition, rolipram especially when combined with adenosine, decreased rhTNF alpha-stimulated PMN adherence to a fibrinogen-coated surface, and the **oxidative burst** of rhTNF alpha-stimulated adherent PMN. The specific adenosine A2a receptor agonists CGS 21680 and WRC-0474 had comparable activity to adenosine in these experiments. Adenosine (or CGS 21680) combined with rolipram synergistically increased f-met-leu-phe-stimulated PMN cAMP content. The effects of both adenosine and rolipram with adenosine could be only partly counteracted by treatment of the PMN with the protein kinase A **inhibitor** KT 5720, indicating that protein phosphorylation is only partially involved. Rolipram activity was about 1000 x (by molar concentration) greater than pentoxifylline in comparable assays. Thus, rolipram, especially when combined with adenosine, has potent modulating effects on PMN activation and may be useful in decreasing inflammatory tissue damage in patients with sepsis.

L33 ANSWER 24 OF 38 MEDLINE DUPLICATE 5
95393637 Document Number: 95393637. PubMed ID: 7664497. Cyclic AMP-elevating agents down-regulate the **oxidative burst** induced by granulocyte-**macrophage** colony-stimulating factor (GM-CSF) in adherent **neutrophils**. Ottonello L; Morone M P; Dapino P; Dallegri F. (Department of Internal Medicine, University of Genova Medical School, Italy.) CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1995 Sep) 101 (3) 502-6. Journal code: 0057202. ISSN: 0009-9104. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Human **neutrophils**, plated on fibronectin-precoated wells, were found to release large quantities of superoxide anion (O2-) in response to GM-CSF. O2- production was reduced by prostaglandin E2 (PGE2) and the phosphodiesterase type IV (PDE IV) **inhibitor** RO 20-1724. Both agents are known to increase intracellular cyclic AMP (cAMP) levels by inducing its production (PGE2) or blocking its catabolism (RO 20-1724). When added in combination, PGE2 and RO 20-1724 had a marked synergistic inhibitory effect, which was reproduced by replacing PGE2 with a direct activator of adenylate cyclase, i.e. forskolin (FK). Moreover, the **neutrophil** response to GM-CSF was inhibited by a

membrane-permeable analogue of cAMP in a dose-dependent manner. As GM-CSF and PGE2 are known to be generated at tissue sites of inflammation, the results suggest the existence of a PGE2-dependent regulatory pathway potentially capable of controlling the **neutrophil** response to GM-CSF, in turn limiting the risk of local oxidative tissue injury. Moreover, owing to its susceptibility to amplification by RO 20-1724, the PGE2-dependent pathway and in particular PDE-IV may represent a pharmacological target to reduce the generation of histotoxic oxidants by GM-CSF-responding **neutrophils**.

L33 ANSWER 25 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 6
95204790 EMBASE Document No.: 1995204790. Signal transduction pathways involved in phagocytic and **oxidative burst** activities of cytokine-treated bovine **neutrophils**. Kabbur M.B.; Jain N.C.. Dept Pathol, Microbiol Immunology, School of Veterinary Medicine, University of California,Davis, CA 95616, United States. Comparative Haematology International 5/1 (38-46) 1995.
ISSN: 0938-7714. CODEN: CHAIEX. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB In vitro studies were conducted to determine the relative importance of various signal transduction factors involved in the phagocytic and **oxidative burst** activities of cytokine-primed bovine **neutrophils**. These **neutrophil** functions were assayed in the presence of known signal transduction pathways **inhibitors** which included nicotinamide, staurosporine, genistein, pertussis toxin, RO 20-1724 and U-73122. **Neutrophils** were isolated (purity > 91%, viability > 97%) from EDTA-anticoagulated jugular blood from five healthy Holstein-Friesian heifers. Freshly isolated **neutrophils** (6 ml, 10 x 106 cells/ml) were incubated separately for 1 h at 37.degree.C with equal volumes of recombinant human cytokines such as tumour necrosis factor-alpha (500 ng/ml), interleukin-1-alpha (1 ng/ml), granulocyte colony-stimulating factor (25 ng/ml), granulocyte-**macrophage** colony-stimulating factor (10 ng/ml) and interferon-gamma (10 ng/ml). Aliquots (1.8 ml) of various cytokine-treated **neutrophils** were exposed to each signal transduction pathways **inhibitor** for 20 min at 37.degree.C in the dark. Then, percentage phagocytosis and average number of intracellular bacteria per cell were evaluated microscopically using FITC-labelled opsonised bacteria (Escheria coli 0111:B4). Unlabelled opsonised bacteria and dichloro-fluorescin diacetate were used to evaluate H2O2 production, a measure of **oxidative burst**, by flow cytometry. Phagocytic activity and H2O2 production by bovine **neutrophils** treated with various cytokines were increased by 52.4-86.1% and 31.3-58.2%, respectively. These functional activities were significantly ($p < 0.05$) reduced after exposure to different **inhibitors** of signal transduction pathways, The reduction in phagocytic activity of cytokine-primed **neutrophils** varied greatly depending on the site of action of various **inhibitors**, with pertussis toxin and U-73122 being the most inhibitory. In comparison, H2O2 production decreased moderately, with pertussis toxin and U-73122 being the most inhibitory and other **inhibitors** inducing minimal variations, It was concluded that G-inhibitory proteins (pertussis toxin-sensitive) and phospholipase C play a major role, whereas tyrosine kinase plays a minor role in the phagocytic activity and H2O2 production by cytokine-primed bovine **neutrophils**.

L33 ANSWER 26 OF 38 MEDLINE DUPLICATE 7
96234418 Document Number: 96234418. PubMed ID: 8699856. Cytokines, phagocytes, and pentoxifylline. Mandell G L. (Division of Infectious Disease, University of Virginia Health Sciences Center, Charlottesville 22908, USA.) JOURNAL OF CARDIOVASCULAR PHARMACOLOGY, (1995) 25 Suppl 2 S20-2. Ref: 7. Journal code: 7902492. ISSN: 0160-2446. Pub. country: United States. Language: English.

AB Phagocytic cells, such as polymorphonuclear **neutrophils**, monocytes, and **macrophages**, are essential for defense against infection caused by a variety of microorganisms. The mechanisms used by these cells to destroy microbes comprise a potent oxidative armamentarium including superoxide, hydrogen peroxide, and hypochlorous acid. In addition, granule contents such as proteolytic enzymes, lysozyme, lactoferrin, and myeloperoxidase are released into the phagosome to destroy ingested microorganisms. Inflammatory cytokines, such as tumor necrosis factor (TNF), interleukin-1 (IL-1), and IL-6, enhance the phagocytic and microbicidal activity of the cells and increase their stickiness. It has been demonstrated in a variety of animal and clinical studies that activated phagocytes can damage the host they are designed to protect, using the mechanisms described above. Alkylxanthines, including pentoxifylline, are potent **inhibitors** of this inflammatory damage by two major actions: (a) reduction of the production of inflammatory cytokines (especially TNF) by phagocytes stimulated with a variety of microbial products (e.g., endotoxin); and (b) reversal of the effect of these cytokines on phagocytes. Thus, pentoxifylline counteracts the following effects of inflammatory cytokines on phagocytes: increased adherence, shape change resulting in larger size and rigidity, increased **oxidative burst**, priming for an enhanced **oxidative burst**, increased degranulation, and decreased chemotactic movement. In addition, these activities synergize with the normal anti-inflammatory mediator adenosine. Alkylxanthines have the potential to be effective therapy for conditions in which inflammatory cytokines and phagocytes cause damage, including the sepsis syndrome, ARDS, AIDS, and arthritis.

L33 ANSWER 27 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
94:554946 The Genuine Article (R) Number: PE520. REGULATION OF INTRACELLULAR POLYMORPHONUCLEAR LEUKOCYTE FC-RECEPTORS BY LIPOPOLYSACCHARIDE. SIMMS H H (Reprint); DAMICO R. BROWN UNIV, RHODE ISL HOSP, SCH MED, DEPT SURG, PROVIDENCE, RI, 02903 (Reprint). CELLULAR IMMUNOLOGY (SEP 1994) Vol. 157, No. 2, pp. 525-541. ISSN: 0008-8749. Pub. country: USA. Language: ENGLISH. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Endotoxemia, in man, has been associated with an autooxidative reduction in the bioavailability of polymorphonuclear leukocyte receptors. The location and mechanisms of this phenomena have remained unclear; we investigated the effects of lipopolysaccharide (LPS) on intracellular Fc gamma receptor expression. Polymorphonuclear leukocytes (PMN) were incubated with LPS (10 ng/ml), permeabilized with saponin, followed by measurement of CD64, CD32w, and CD16 (Fc gamma RI, II, III) using I-125-monoclonal antibodies directed against these receptors. Exposure of permeabilized PMN to LPS significantly reduced intracellular Fc gamma receptor expression. PMN isolated from patients with chronic granulomatous disease or myeloperoxidase-specific deficiency did not exhibit this effect. Furthermore, specific **inhibitors** of components of the PMN **oxidative burst** (N2N3, 10 mM;L-alanine 30 mM) prevented the LPS-induced oxidative reduction in receptor expression. NADPH oxidase inhibition with diphenyleneiodonium also blocked the effect of LPS on intracellular Fc gamma receptor expression. The effects of LPS on intracellular PMN Fc gamma receptors were reproduced with monophosphoryl lipid A but required a 10 times greater concentration than LPS. Preadherence of PMN on fibronectin or arginine-glycine-aspartate-serine (RGDS), but not laminin, prevented the LPS-induced reduction in oxidative receptor expression. The effects of fibronectin/RGDS were blocked by actinomycin D and cycloheximide. Cross-linkage of intracellular Fc gamma receptors prior to exposure to LPS also prevented the LPS-induced oxidative reduction in receptor expression. These results demonstrate that an important pathophysiologic property of LPS is to induce an intracellular oxidative-derived reduction in Fcr receptor expression and that the biologically relevant proteins fibronectin and RGDS ameliorate

this effect. (C) 1994 Academic Press, Inc.

L33 ANSWER 28 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
94325408 EMBASE Document No.: 1994325408. Regulation of platelet-derived growth factor (PDGF) and alveolar **macrophage**-derived PDGF by .alpha.2-macroglobulin. Bonner J.C.. Laboratory of Pulmonary Pathobiology, Natl Institute Environmental Health,Research Triangle Park, NC 27709, United States. Annals of the New York Academy of Sciences 737/- (324-338) 1994.
ISSN: 0077-8923. CODEN: ANYAA. Pub. Country: United States. Language: English. Summary Language: English.
AB In vitro findings suggest that .alpha.2M is an important regulator of PDGF-stimulated fibroblast proliferation and chemotaxis. Native .alpha.2M binds to PDGF and prevents PDGF from interacting with its receptor, but serves as an extracellular reservoir for the growth factor, which can be released over time in a controlled fashion to interact with the PDGF-.alpha. or -.beta. receptor. Methylamine-activated .alpha.2M synergistically enhances PDGF-induced cell growth, whereas plasmin-activated .alpha.2M inhibits PDGF-stimulated fibroblast proliferation. The reason for the difference in the effect of these two receptor-recognized .alpha.2Ms is unknown. PDGF secreted by rat alveolar **macrophages** is bound to homologues of human .alpha.2M and it has been suggested that PDGF action in the lung is tightly controlled during normal tissue remodeling. It is important to consider another regulator of PDGF termed SPARC (secreted protein, acidic and rich in cysteine), which inhibits the binding of PDGF-BB and -AB to cell-surface PDGF-.beta. receptors. SPARC could modulate PDGF activity during inflammation and tissue repair by limiting the availability of dimers containing the PDGF B chain. Future studies should address the relative importance of SPARC and .alpha.2M in regulating PDGF-induced chemotaxis and proliferation. During inflammation or during the progression of fibroproliferative lung disease, the regulation of PDGF might be lost. For example, **oxidative bursts** from inflammatory cells (**neutrophils** and eosinophils) functionally inactivate .alpha.2M. Thus, inhaled environmental insults (particles and oxidants) could perturb the normal growth regulatory signaling system between cells via the network that includes cytokines, .alpha.2M, and proteinases.

L33 ANSWER 29 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
93:205273 The Genuine Article (R) Number: KU320. ENHANCEMENT OF OXIDATIVE RESPONSE AND DAMAGE CAUSED BY HUMAN **NEUTROPHILS** TO ASPERGILLUS-FUMIGATUS HYPHAE BY GRANULOCYTE COLONY-STIMULATING FACTOR AND GAMMA INTERFERON. ROILIDES E; UHLIG K; VENZON D; PIZZO P A; WALSH T J (Reprint). NCI, INFECT DIS SECT, PEDIAT BRANCH, BETHESDA, MD, 20892; NCI, BIOSTAT & DATA MANAGEMENT SECT, BETHESDA, MD, 20892. INFECTION AND IMMUNITY (APR 1993) Vol. 61, No. 4, pp. 1185-1193. ISSN: 0019-9567. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Invasive aspergillosis is a serious fungal infection caused by the proliferation and invasion of Aspergillus hyphae in tissue. **Neutrophils** (PMNs) are the most important line of defense against Aspergillus hyphae. To investigate the role of granulocyte colony-stimulating factor (G-CSF) and gamma interferon (IFN-gamma) against Aspergillus fumigatus, we studied the effects of the two cytokines on the **oxidative burst** and the capacity of normal human PMNs to damage hyphae of the organism. G-CSF enhanced PMN **oxidative burst** measured as superoxide anion (O2-) production in response to N-formylmethionyl leucyl phenylalanine, serum opsonized hyphae, and nonopsonized hyphae by 75, 37, and 24%, respectively, compared with control PMNs ($P < 0.015$). IFN-gamma also induced increases of 52, 71, and 96%, respectively, in response to the same stimuli ($P < 0.006$). In addition, the capacity of PMNs to damage hyphae as measured by the

3-4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MMT) colorimetric metabolic assay was significantly enhanced by G-CSF and IFN-gamma ($P < 0.01$ and < 0.05, respectively). The enhancement was achieved irrespective of serum opsonization of the hyphae, suggesting upregulatory actions of the two cytokines on signal pathways specific for opsonized and nonopsonized hyphae. The combination of the two cytokines exhibited an additive effect at the higher concentrations compared with the effects of the cytokines alone ($P < 0.05$). Pretreatment of PMNs with protein synthesis **inhibitors** showed that IFN-gamma activates PMN function through transcriptional regulation, whereas the effect of G-CSF does not require new proteins. These in vitro effects suggest modulatory roles for G-CSF and IFN-gamma in the host defense against Aspergillus hyphae irrespective of serum opsonization and a potential utility of the cytokines as adjuncts for the prevention and possible treatment of invasive aspergillosis.

L33 ANSWER 30 OF 38 CAPLUS COPYRIGHT 2003 ACS
1994:499293 Document No. 121:99293 Modulation of secretory processes of phagocytes by IX 207-887. Schnyder, Joerg; Cooper, Philip; MacKenzie, Andrew (Sandoz Res. Inst. Berne Ltd., Bern, CH-3001, Switz.). Springer Seminars in Immunopathology, 14(4), 345-52 (English) 1993. CODEN: SSIMDV. ISSN: 0344-4325.

AB In chronic inflammation, the mediators released by phagocytes are in part responsible for the initiation and perpetuation of the disease. IX 207-887, which is a novel antiarthritic drug, inhibits the release of cytokines from mononuclear cells at concns. which are achieved therapeutically in human rheumatoid arthritis and in animal models of arthritis. Furthermore, the prodn. of superoxide and release of azurophil and specific granules by N-formyl-Met-Leu-Phe-stimulated **neutrophils** are significantly reduced. As a consequence, IX 207-887 may break the vicious circle which is manifest in chronic inflammation. In a recent double-blind placebo controlled study IX 207-887 has been shown to be an effective slow-acting drug for use in rheumatoid arthritis.

L33 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2003 ACS
1991:605767 Document No. 115:205767 Effect of a factor released by K562 malignant cells in culture on human **neutrophil** bactericidal activity. Amar, Michele; Amit, Norma; Babin-Chevaye, Catherine; Pham Huu Trung; Hakim, Jacques (Lab. Hematol. Immunol. Biol., CHU Xavier Bichat, Paris, 75877, Fr.). Infection and Immunity, 59(8), 2673-6 (English) 1991. CODEN: INFIBR. ISSN: 0019-9567.

AB It was previously demonstrated that K562 malignant cells in culture contain and release a low-mol.-mass (8-kDa) factor that inhibits adherence-related functions of **neutrophils** but does not alter fMet-Leu-Phe- or phorbol ester-induced **oxidative burst**. The present study investigated the effects of this factor, referred to as inhibitory factor 1 (IF1), on the bactericidal activity of human polymorphonuclear cells (PMNs) on Staphylococcus aureus opsonized in various ways. S. aureus was used either nonopsonized or opsonized with heat-inactivated serum or normal serum contg. complement factors. The bactericidal activity of PMNs preincubated with IF1-treated or control medium was examd. by counting the surviving bacteria. The ability of IF1-treated PMNs to kill bacteria was diminished when they were opsonized with normal serum. When S. aureus was not opsonized or was opsonized with heat-inactivated serum, the bactericidal activity of IF1-treaetd PMNs was similar to that of controls. Likewise, the phagocytosis of IF1-treated PMNs was diminished when S. aureus was opsonized with normal serum but was not altered when S. aureus was not opsonized or was opsonized with heat-inactivated serum. These results suggest that the decrease in killing might be due to defective ingestion. The chemiluminescence response of IF1-treated PMNs was inhibited when S. aureus was not

opsonized or was opsonized with normal serum. These results suggest that IF1 interferes not only with S. aureus stimulation of PMNs via complement receptors but also with oxygen-dependent bactericidal activity.

L33 ANSWER 32 OF 38 MEDLINE DUPLICATE 8
91166598 Document Number: 91166598. PubMed ID: 1848432. Crystal-induced **neutrophil** activation. I. Initiation and modulation of calcium mobilization and superoxide production by microcrystals. Naccache P H; Grimard M; Roberge C J; Gilbert C; Lussier A; de Medicis R; Poubelle P E. (Department de Medicine, Universite Laval, Ste Foy, Quebec, Canada.) ARTHRITIS AND RHEUMATISM, (1991 Mar) 34 (3) 333-42. Journal code: 0370605. ISSN: 0004-3591. Pub. country: United States. Language: English.
AB The effects of monosodium urate and calcium pyrophosphate dihydrate crystals on the levels of cytoplasmic free calcium and on the **oxidative burst** in normal human blood **neutrophils** were examined. The pattern of sensitivity to granulocyte-**macrophage** colony-stimulating factor, colchicine, cytochalasin B, pertussis toxin, diglyceride kinase, and protein kinase C **inhibitors** differentiated the mechanism(s) of **neutrophil** activation by the crystals from that involved in the responses to soluble chemotactic factors and indicated that individual crystals can use several activation pathways.

L33 ANSWER 33 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
91:198517 The Genuine Article (R) Number: FE320. AVOIDANCE, AND INACTIVATION OF REACTIVE OXYGEN SPECIES - NOVEL MICROBIAL IMMUNE EVASION STRATEGIES. EZE M O (Reprint). UNIV NIGERIA, DEPT BIOCHEM, NSUKKA, NIGERIA (Reprint). MEDICAL HYPOTHESES (1991) Vol. 34, No. 3, pp. 252-255. Pub. country: NIGERIA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB A prominent aspect of host cell-mediated immune (CMI) reactions leading to the clearance of infections is the production of one or more reactive oxygen species (ROS) such as superoxide (O2-), hydrogen peroxide (H2O2), hydroxyl radical (OH.), and hypohalite (e.g., OCl-). These ROS are usually produced by phagocytes. A number of chemotherapeutic agents also produce ROS in the process of their curative mechanisms. In a variety of infections, these ROS constitute a formidable arsenal in the clearance of the infection. In some cases, the excess ROS could also cause tissue damage.

Evidence is herewith presented that pathogenic intracellular microorganisms, in order to enhance their survival as well as effective virulence within the host, have evolved novel strategies in the nature of avoidance, or inhibition of ROS production by phagocytes, or neutralization of already produced ROS. It is advocated that more in depth studies be undertaken in these respects in order to be able to exploit these phenomena in the production of more efficacious chemotherapeutic agents and anti-pathogen vaccines.

L33 ANSWER 34 OF 38 MEDLINE
92089493 Document Number: 92089493. PubMed ID: 1751754. Priming of phagocytes by cytokines and water-soluble products of lipid peroxidation. Koval'chuk L V; Klebanov G I; Ribarov S R; Kreinina M V; Aptsiauri N E; Gankowskaya L W; Karaseva M V; Shuikina E E; Vladimirov YuA. (Department of Immunology, 2nd Moscow State Medical Institute.) BIOMEDICAL SCIENCE, (1991) 2 (3) 221-31. Journal code: 9010320. ISSN: 0955-9701. Pub. country: ENGLAND: United Kingdom. Language: English.
AB It is well known that during certain pathological processes phagocytes acquire the ability to generate activated oxygen species during phagocytosis. The priming of phagocytes by cytokines and water-soluble products of lipid peroxidation (LPO) is described. Preincubation of human polymorphonuclear leukocytes (PMNL) with the water-soluble products of LPO or oxidised liposomes for 15-20 min at 37 degrees C enhanced their

functional activity when they were stimulated by opsonised zymosan or latex particles. There was a 2-3-fold increase in luminol-dependent chemiluminescence response of cells stimulated in this way, and an increase in Fc-receptor expression on the PMNL surface. An endogenous cytokine alone did not activate the phagocytes for an **oxidative burst** response, but preincubation of murine peritoneal **macrophages** (MP) and human PMNL with cytokines (molecular mass 20-30 kDa) for 3-48 h at 37 degrees C enhanced the cell chemiluminescence response to opsonised zymosan by a factor of 5-9 for MP and a factor of 2-3 for PMNL. Treatment of phagocytes with the cytokine complex also increased other effector functions of the phagocytes such as tumouricidal activity, phagocytosis, secretion of interleukin-1, and antiparasitic activity. The protein synthesis **inhibitor** cycloheximide abolished cytokine-induced priming of MP (but not of PMNL). The mechanisms of short-term and prolonged priming of the two types of phagocytes (MP and PMNL) are discussed.

L33 ANSWER 35 OF 38 MEDLINE DUPLICATE 9
90366707 Document Number: 90366707. PubMed ID: 2168226.
Isoquinolinesulfonamide protein kinase **inhibitors** H7 and H8 enhance the effects of granulocyte-**macrophage** colony-stimulating factor (GM-CSE) on **neutrophil** function and inhibit GM-CSF receptor internalization. Khwaja A; Roberts P J; Jones H M; Yong K; Jaswon M S; Linch D C. (Department of Haematology, University College Middlesex School of Medicine, London, UK.) BLOOD, (1990 Sep 1) 76 (5) 996-1003. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB Human granulocyte-**macrophage** colony-stimulating factor (GM-CSF) increases **neutrophil** surface expression of the cellular adhesion molecule CD11b and primes the respiratory burst stimulated by the bacterial peptide f-met-leuphe (FMLP). We have examined the effects of the isoquinolinesulfonamide protein kinase **inhibitors** H7 and H8 on these functions of GM-CSF using whole blood assays. Concentrations of H7 and H8 that inhibited the 12-O-tetradecanoyl-phorbol-13-acetate (TPA) stimulated upregulation of CD11b expression and activation of the respiratory burst, both augmented the effects of GM-CSF. H7 and H8 enhanced the GM-CSF-stimulated increase in CD11b expression to 215% +/- 10% (P less than .05) and 233% +/- 45% (P less than .05), respectively, of the value obtained with GM-CSF alone. The GM-CSF priming of the FMLP-stimulated **oxidative burst** was increased to 190% +/- 44% (P less than .01) by preincubation with H7 and to 172% +/- 25% (P less than .01) with H8. Preincubation with H8 did not affect overall binding of 125I-GM-CSF to **neutrophils**, but inhibited GM-CSF receptor internalization after ligand binding (P less than .05). These data indicate that the effects of GM-CSF are not mediated by protein kinase C and that a phosphorylation event down-modulates the **neutrophil** response to GM-CSF. It suggests that internalization of the receptor-ligand complex is not a rate-limiting step in signal transduction, and that regulation of the rate of internalization may be an important level of control of the activity of GM-CSF.

L33 ANSWER 36 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
90069237 EMBASE Document No.: 1990069237. **Macrophages** and polymorphonuclear **neutrophils** in lung defense and injury.
Sibille Y.; Reynolds H.Y.. Pulmonary Section, Catholic University of Louvain, Louvain, Belgium. American Review of Respiratory Disease 141/2 I (471-501) 1990.
ISSN: 0003-0805. CODEN: ARDSBL. Pub. Country: United States. Language: English. Summary Language: English.

AB Phagocytes, in particular **macrophages** and PMN, are now recognized as major components of inflammatory and immunologic reactions in the lung. Normally, **macrophages** represent the majority of

phagocytes in the lower respiratory tract. These lung **macrophages** are morphologically and functionally heterogenous and include alveolar, interstitial, intravascular, and airway **macrophages**, each with characteristic morphologic and functional features. Through the presence of surface receptors for numerous ligands and through their large number of secretory products, lung **macrophages** can respond to environmental factors and account for most of the clearance of microparticles and microorganisms in the distal airways and the alveolar spaces. In addition, **macrophages** also play an important role in inflammatory processes through the release of oxygen radicals and proteolytic enzymes. Through the release of several cytokines, i.e., growth-promoting and inhibiting factors, lung **macrophages** may also influence both matrix damage and repair processes. **Macrophages** can also contribute to the alveolitis by recruitment of inflammatory and immune cells. This latter contribution is best demonstrated in migration movement of PMN. The normal distal airways generally contain a small number of PMN, but the pulmonary vascular bed represents a large reservoir of PMN. Some of them are in intimate contact with the endothelium, forming the so-called marginating pool of PMN. Because the capillary lumen is separated only from the alveolar space by a monolayer of endothelial and epithelial cells on each side of a thin interstitial matrix, it is likely that some inhibitory mechanism exists to prevent PMN from migrating towards the alveolar space. Such **inhibitors** of PMN migration are present both in serum and in the alveolar space, some being released by alveolar **macrophages**. However, alveolar **macrophages** can also secrete factors called chemotaxins that attract PMN to the airways, and this supports a central role for alveolar **macrophages** in the regulation of PMN traffic in the lungs. Thus, secretory products of alveolar **macrophages** are part of the regulatory mechanisms of PMN mobility and adherence that appears to be crucial in the initiation of some inflammatory reactions. The contribution of phagocytes to the defense against infection and tumor has been documented mostly in vitro. Thus, both oxygen radicals, in particular hydroxyl radicals and proteases such as lysozyme, are potent bactericidal agents. That phagocytes are also important defenders of the lungs in vivo is best supported by the observations in immunodeficient patients and animal models. Patients with leukopenia and animals may suffer life-threatening infections often involving the lungs. Also, specific defects in phagocyte functions such as in chronic granulomatous disease (lack of **oxidative burst**) or in alveolar proteinosis (impaired phagocytosis by **macrophages**) are associated with severe infectious problems. In addition to their major defensive role, phagocytes occasionally can be associated with injurious processes, especially in the lung, and this appears to result from an inadequate or unrestrained activation of either **macrophages** or PMN or both. Again, this is mostly substantiated by in vitro studies. However, studies in emphysema and in idiopathic pulmonary fibrosis suggest that oxidants and proteases (including elastase) derived from PMN and probably from alveolar **macrophages** contribute in vivo to lung matrix degradation. In conclusion, alveolar **macrophages** and PMN participate in both defense and injury processes of the lungs. As the resident phagocyte of the lower respiratory tract, the **macrophage** is a versatile cell with paradoxical effects, able to release oxidants, proteolytic enzymes, and mediators, but also able to secrete antioxidants, antiproteases, and **inhibitors** of cytokines. By contrast, the PMN is virtually absent from the alveoli (approximately 1% of normal, nonsmoker bronchoalveolar cells). However, when recruited in inflammatory states, PMN can outnumber **macrophages** and release substantial amounts of oxygen species and enzymes. Hence, phagocytes represent only one component of a complex network of cellular and humoral factors interacting in defense, injury, and immune reaction. Lymphocytes, platelets, eosinophils, fibroblasts, epithelial and endothelial cells are

also implicated in lung injury and repair, either independently or synergistically with **macrophages** and/or PMN. In particular, through the release of lymphokines, lymphocytes appear to play a central role in the regulation of both **macrophages** and PMN function in interstitial lung diseases. This role may vary considerably depending on the triggering agent(s), unknown in most cases.

L33 ANSWER 37 OF 38 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
1990:132434 Document No.: BA89:71245. POSTBURN SUPPRESSION OF MURINE LYMPHOCYTE AND **NEUTROPHIL** FUNCTIONS IS NOT REVERSED BY PROSTAGLANDIN BLOCKADE. GADD M A; HANSBROUGH J F. DEP. SURG. H640B, UNIV. CALIFORNIA SAN DIEGO MED. CENT., 225 DICKINSON ST., SAN DIEGO, CALIF. 92103, USA.. J SURG RES, (1990) 48 (1), 84-90. CODEN: JSGRA2. ISSN: 0022-4804. Language: English.

AB Certain arachidonic acid metabolites, including prostaglandins (PGs) E1 and E2, have been shown to exert marked immunosuppressive effects on T-cell and **macrophage** functions. Cyclooxygenase blockade with indomethacin or ibuprofen may ameloriate these effects. In the current study we measured lymphocyte proliferation by thymidine incorporation, the presence of T-cell activation antigens with monoclonal antibodies and two-color flow cytometry, and **neutrophil** (PMN) **oxidative burst** using a fluorescent marker, in control mice and in burned mice treated with indomethacin for 10 days after injury. One-half of the cell cultures were treated with indomethacin in vitro to ensure its continued presence during stimulation. Separate groups of mice were fed a fish oil-based diet which leads to the production of PGE3 rather than PGE2, versus standard mouse chow, a soy-bean oil-based diet which leads to PGE2 production. Lymphocyte proliferation, expression of T-cell activation antigens, and PMN **oxidative burst** remained depressed in burned mice treated with indomethacin in vivo (plus in vitro) and in those which received the fish oil-based diet, compared to control. Blockade of PG synthesis after murine burn injury by cyclooxygenase inhibition or alterations in the diet failed to restore T-lymphocyte activation or proliferation or to improve PMN **oxidative burst**. These data suggest that PGE2 alone does not explain the immunosuppression noted after burn injury.

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89335802 Document Number: 89335802. PubMed ID: 2758063. Control of exogenous proteinases and their **inhibitors** at the **macrophage** cell surface. Dean R T; Schnebli H P. (Ciba-Geigy, Basel, Switzerland.) BIOCHIMICA ET BIOPHYSICA ACTA, (1989 Aug 18) 992 (2) 174-80. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB The actions and availability of human **neutrophil** elastase and its protein **inhibitor**, Eglin, when co-incubated with **macrophages** were investigated. Eglin did not induce radical production by mouse peritoneal **macrophages**; nor were specific binding sites for Eglin detected on these cells. Mouse peritoneal **macrophages** could inactivate both elastase and Eglin extensively, when these targets were used at concentrations appropriate to the extravascular fluids. Two methods were used for assessing such inactivation: one, as in previous literature, only took account of molecules remaining in the supernatant after interaction with the cells; the other (lacking from most previous studies) took into account all target molecules, including those associated with the cells. From an analysis of both types of experiment, it was shown that the cell-derived inactivators were stable products, whose quantity was not significantly influenced by the induction of a **macrophage oxidative burst** and its associated free radicals. They were probably mainly proteinases and proteinase **inhibitors**. Thus, mouse peritoneal **macrophages** restrict the activity of proteinases and

inhibitors by means of stable molecules, such as proteins. Other mononuclear phagocytes may use free radicals and oxidants more extensively in this respect.

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